

O I P E
DEC 13 2004

PATENT & TRADEMARK OFFICE
U.S. GOVERNMENT

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STEP : 0.050° CNT TIME: 1.000 SEC.
RANGE: 2.00 - 40.00 (DEG) CONT. SCAN RATE : 3.00 DEG/MIN.

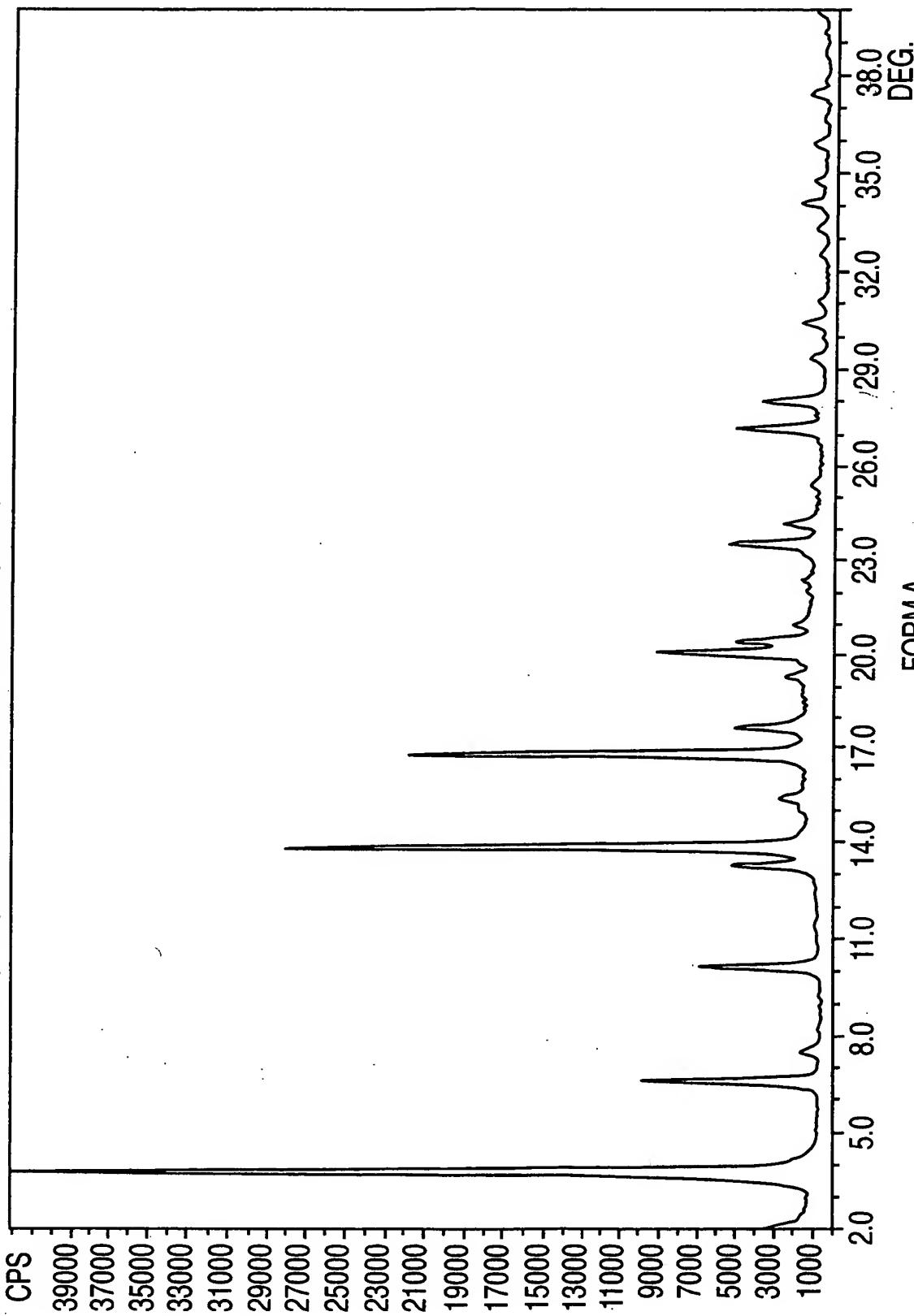
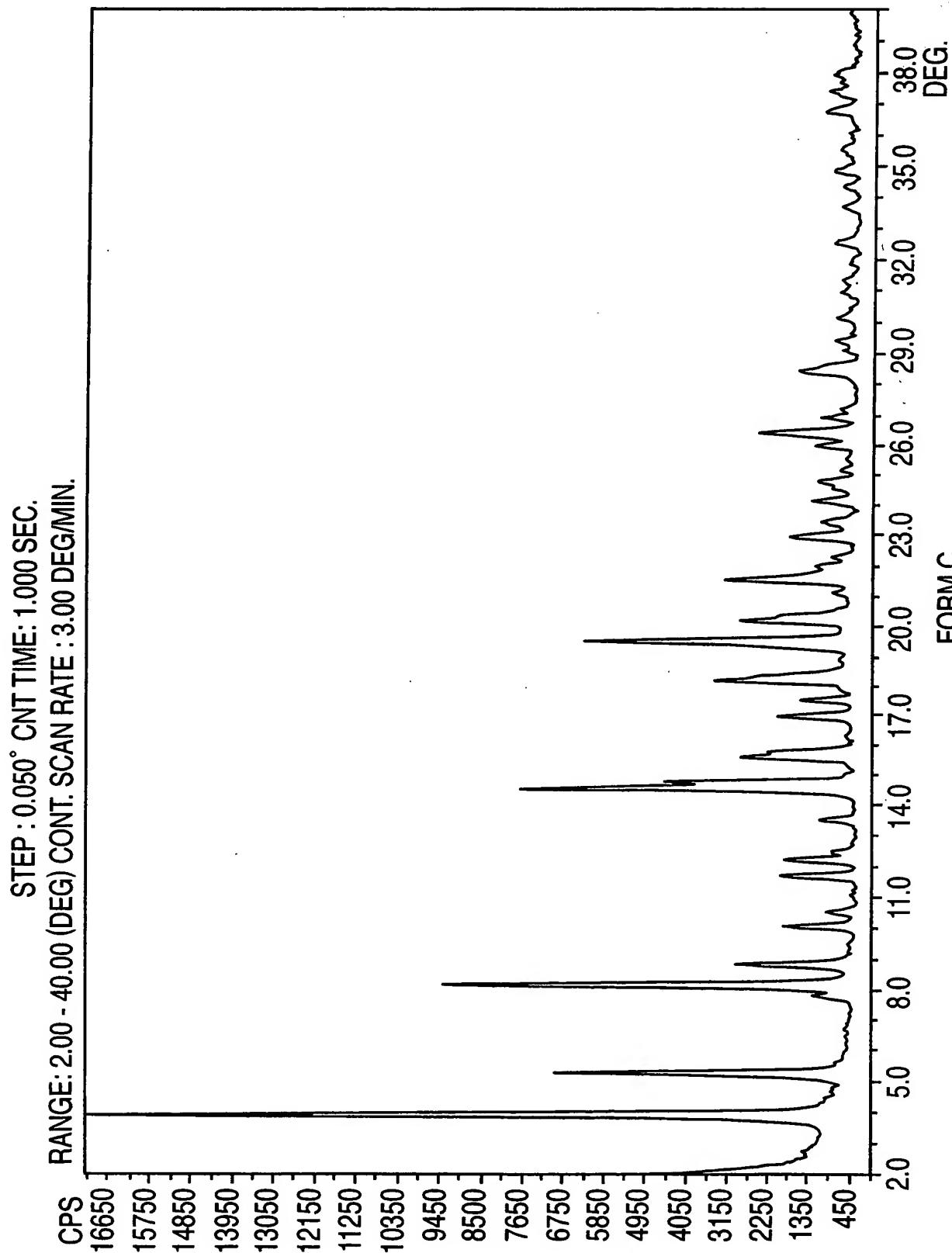


FIG. 1
FORM A



FORM C
FIG. 2

STEP : 0.050° CNT TIME: 1.000 SEC.
RANGE: 2.00 - 40.00 (DEG) CONT. SCAN RATE : 3.00 DEG/MIN. TEVA

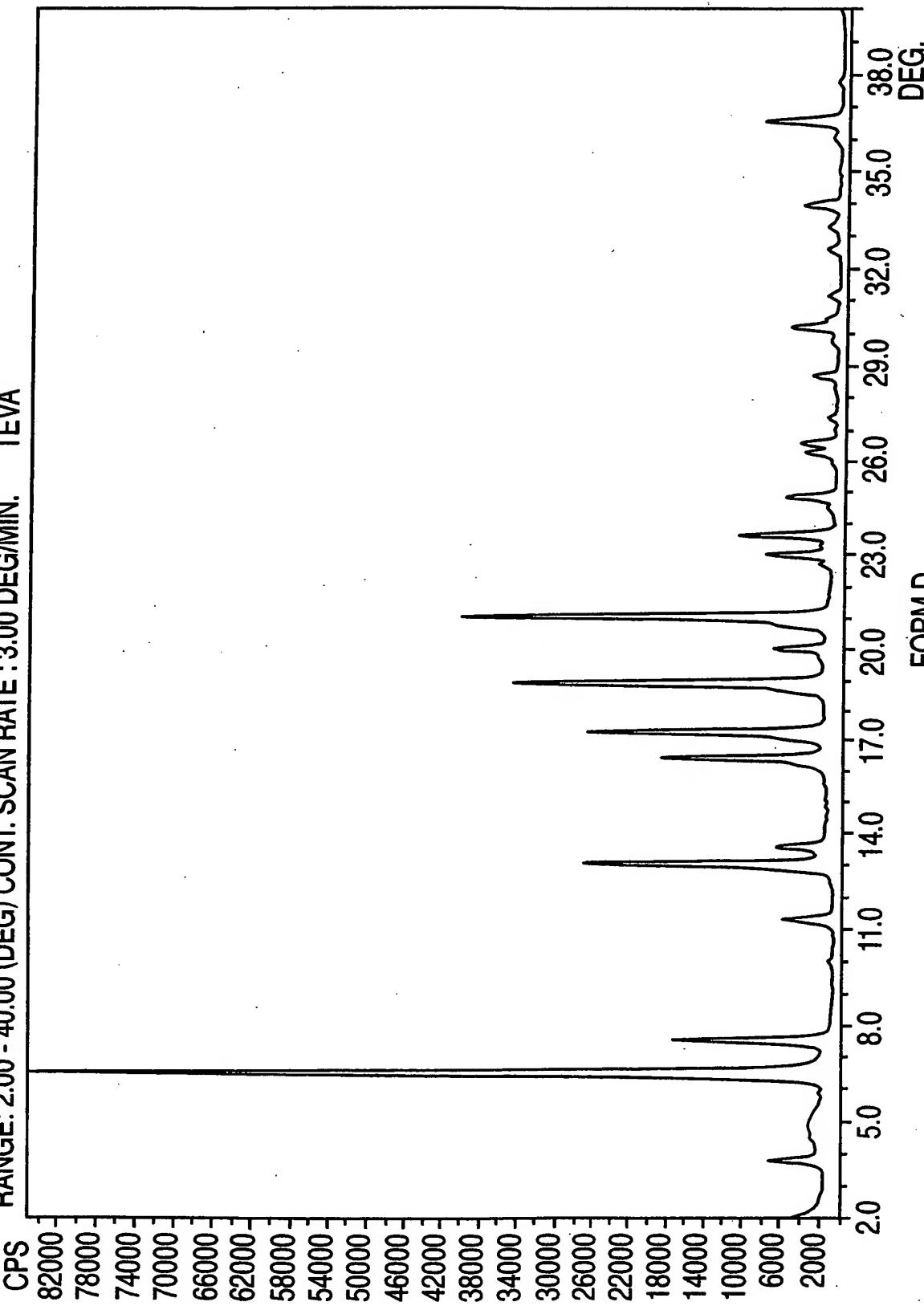


FIG. 3
FORM D

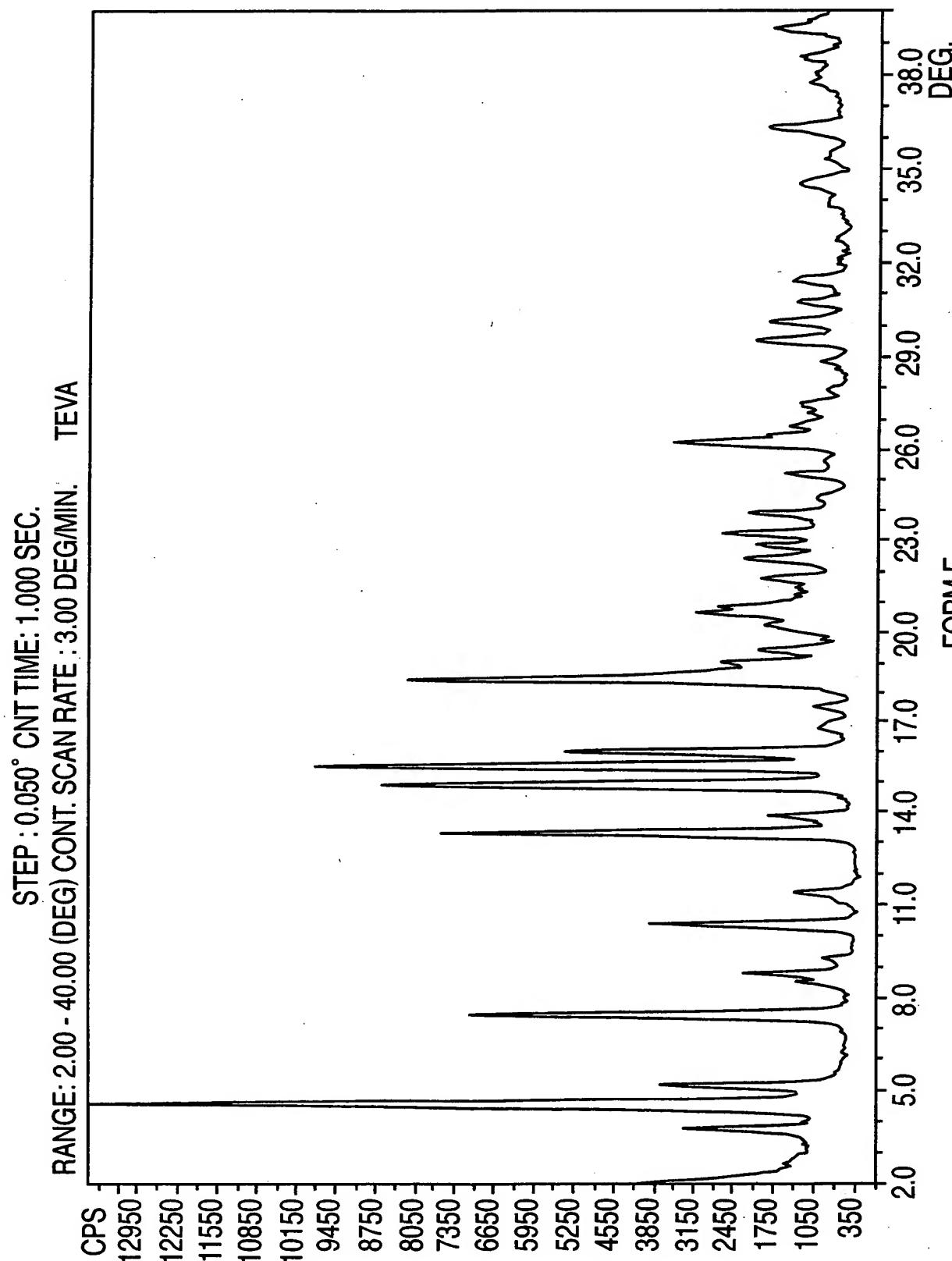


FIG. 4
FORM E

STEP : 0.05° CNT TIME: 1.000 SEC.
RANGE: 2.00 - 40.00 (DEG) CONT. SCAN RATE : 3.00 DEG/MIN.

CPS

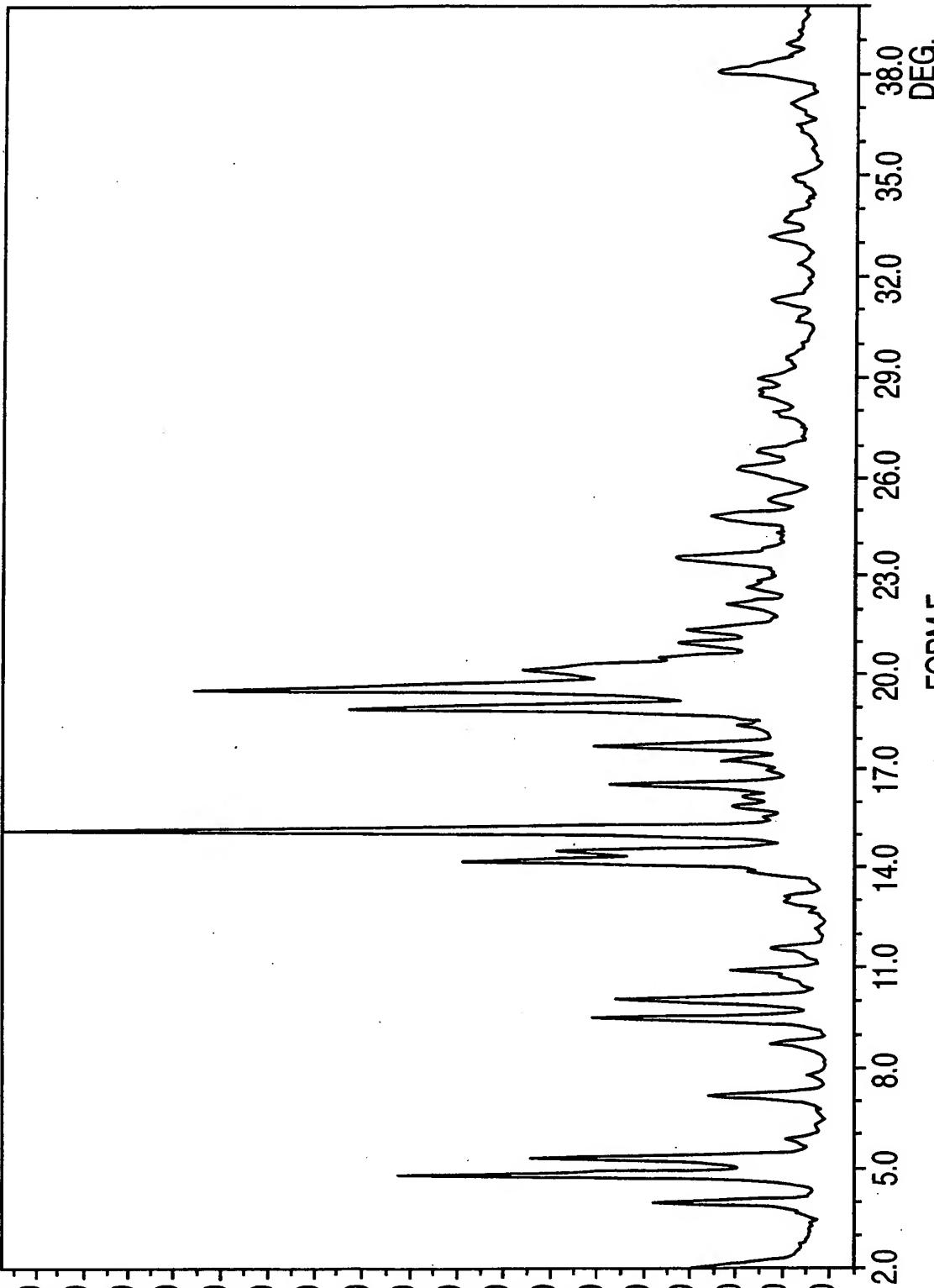
⊕

21000
19800
18600
17400
16200
15000
13800
12600
11400
10200
9000
7800
6600
5400
4200
3000
1800
600

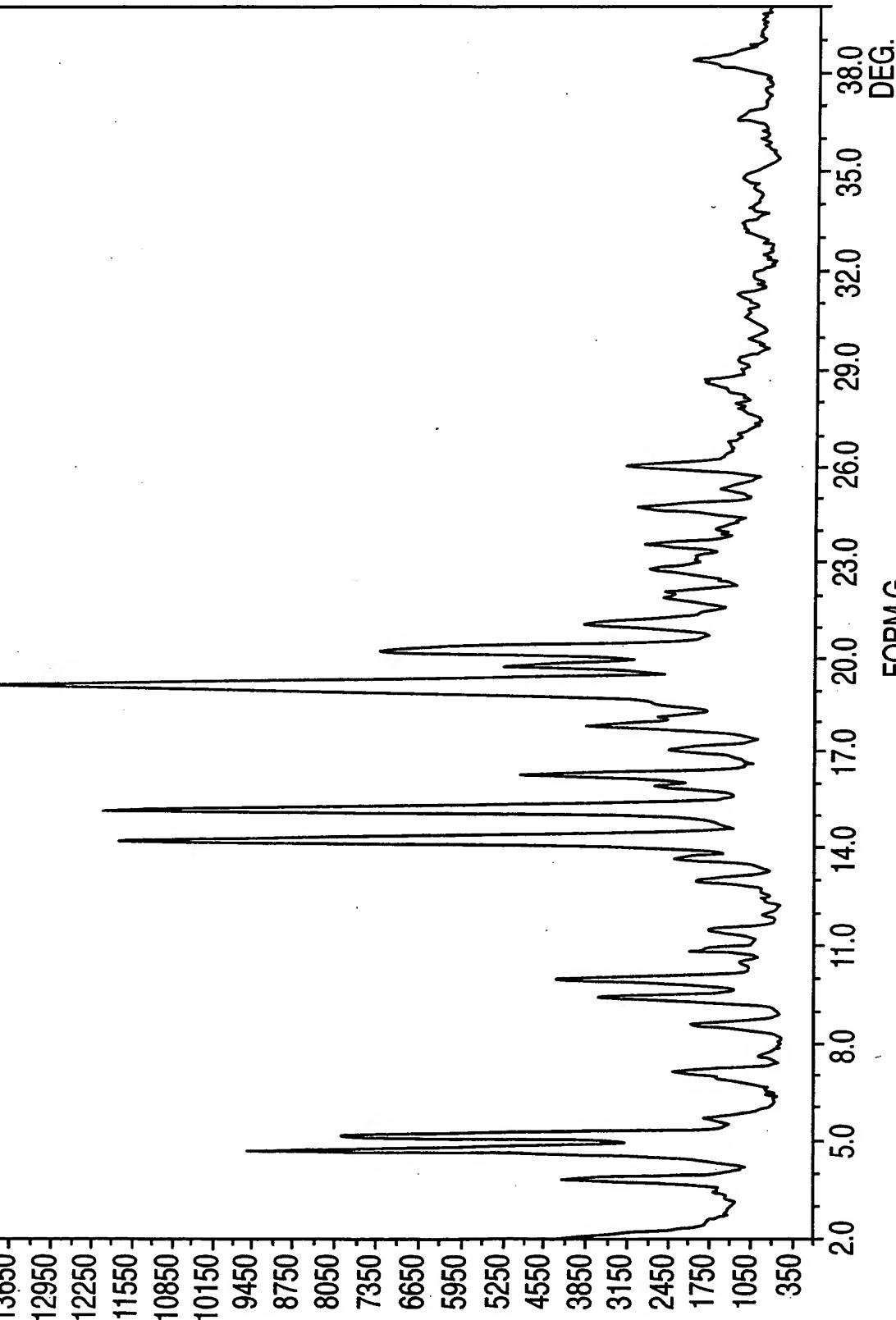
FIG. 5
FORM F

DEG.

38.0
35.0
32.0
29.0
26.0
23.0
20.0
17.0
14.0
11.0
8.0
5.0
2.0



STEP : 0.050° CNT TIME: 1.000 SEC.
RANGE: 2.00 - 40.00 (DEG) CONT. SCAN RATE : 3.00 DEG/MIN.



⊕

FIG. 6
FORM G

STEP : 0.05° CNT TIME: 1.000 SEC.
RANGE: 2.00 - 40.00 (DEG) CONT. SCAN RATE : 3.00 DEG/MIN. TEVA

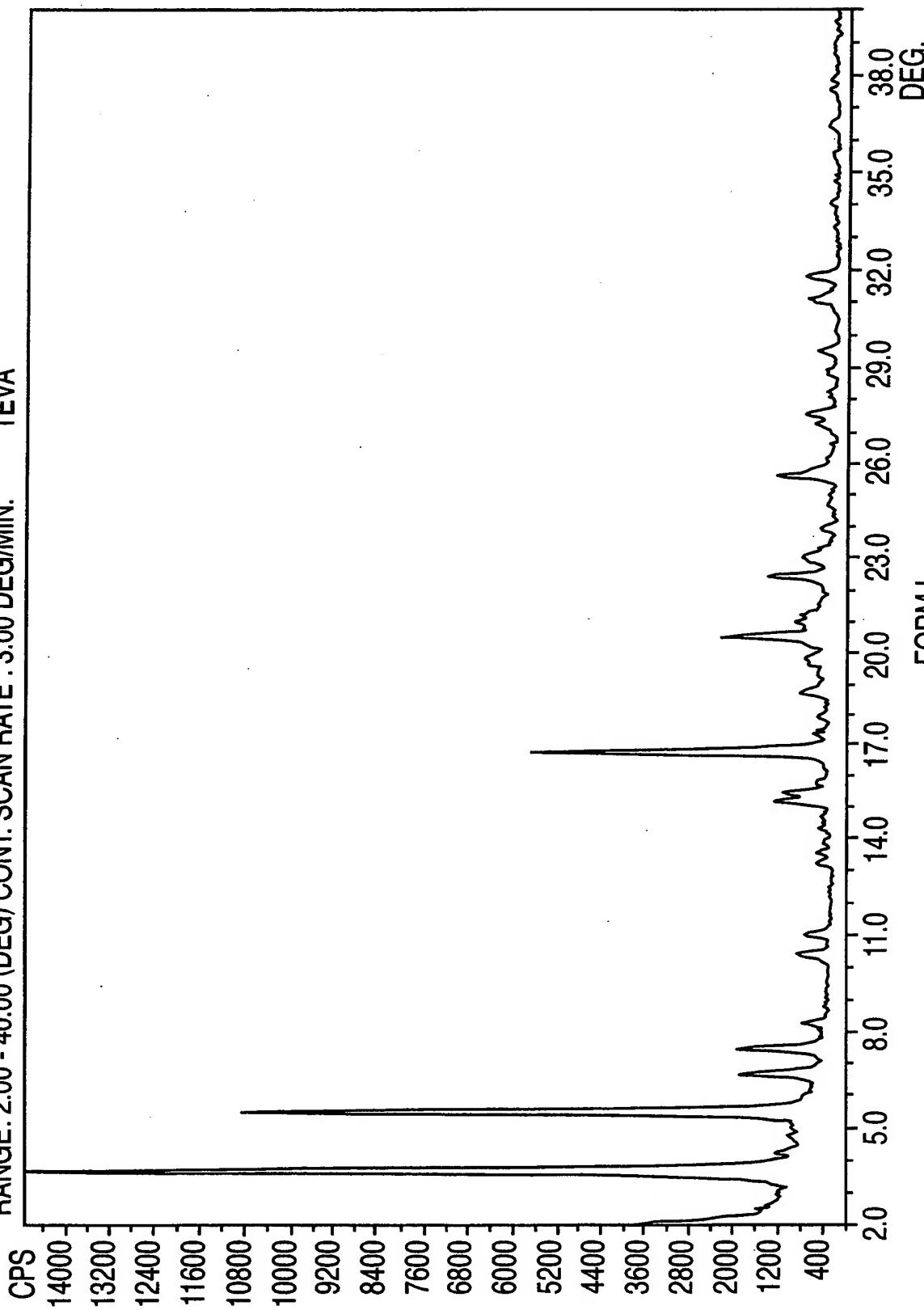
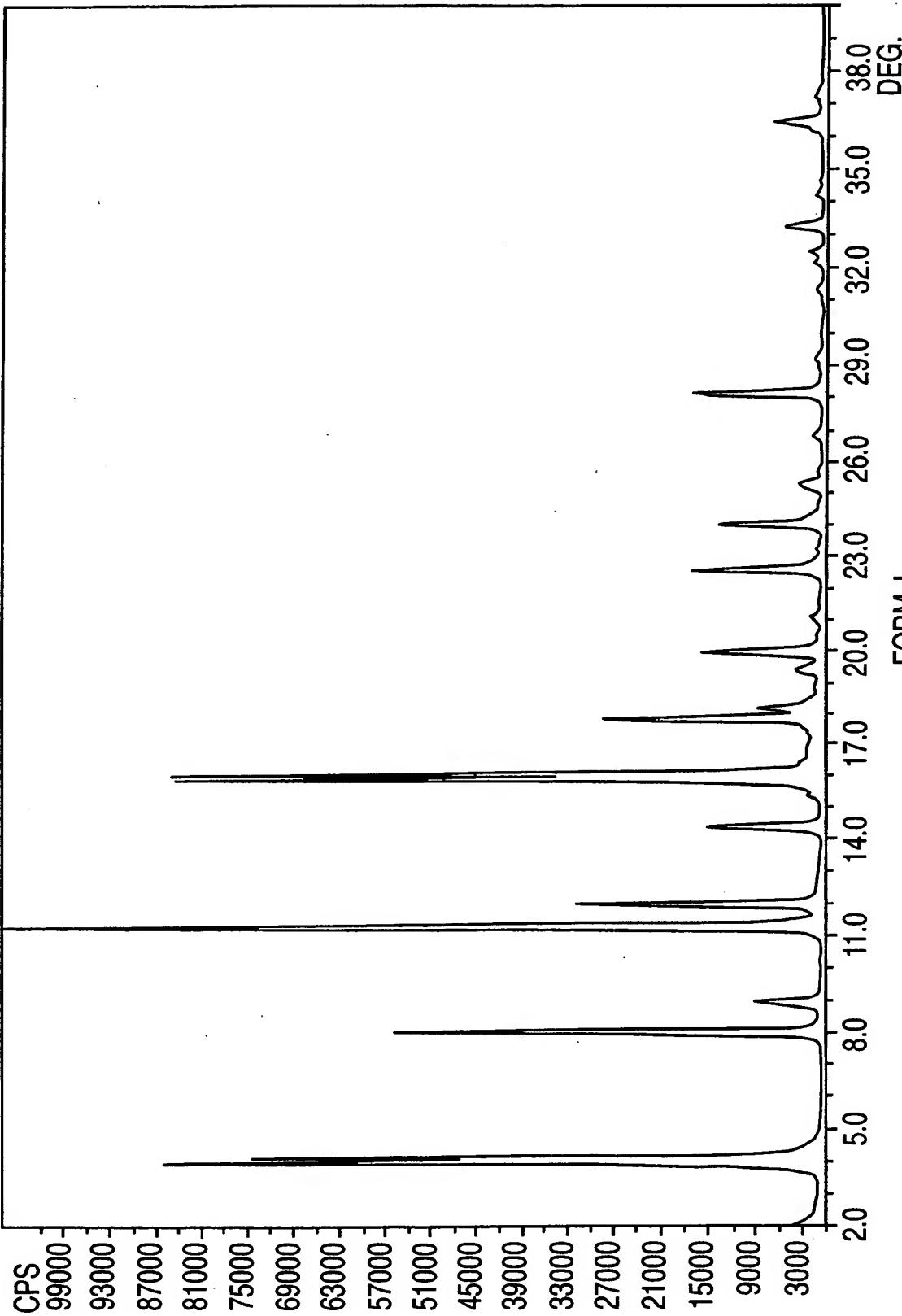


FIG. 7
FORM I

STEP : 0.050° CNT TIME: 1.000 SEC.
RANGE: 2.00 - 40.00 (DEG) CONT. SCAN RATE : 3.00 DEG/MIN.



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FIG. 8
FORM J

STEP : 0.050° CNT TIME: 1.000 SEC.
RANGE: 2.00 - 40.00 (DEG) CONT. SCAN RATE : 3.00 DEG/MIN.

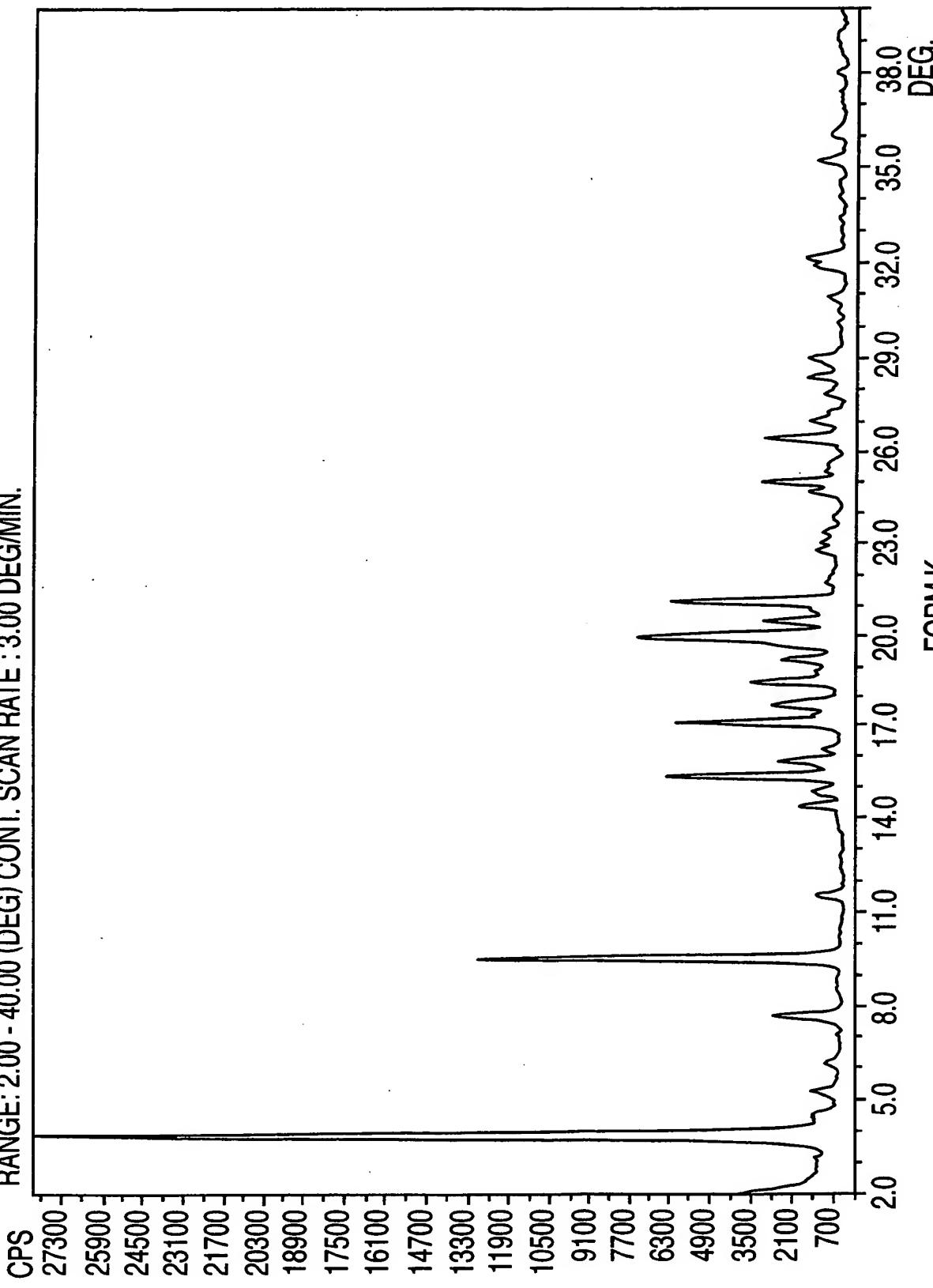


FIG. 9

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STEP : 0.050° CNT TIME: 1.000 SEC.
RANGE: 2.00 - 40.00 (DEG) CONT. SCAN RATE : 3.00 DEG/MIN.

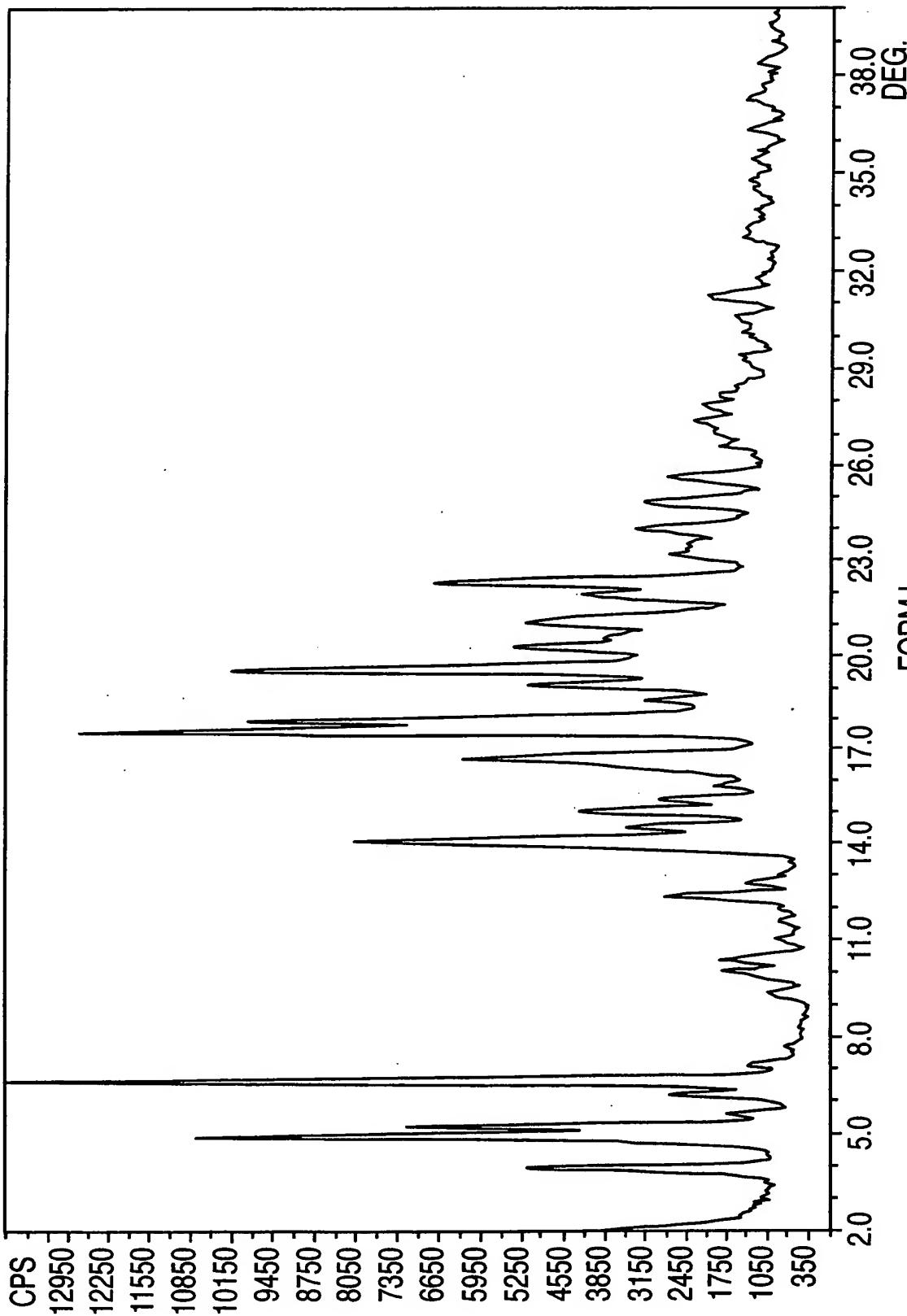


FIG. 10
FORM L

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STEP : 0.050° CNT TIME: 1.000 SEC.
RANGE: 2.00 - 40.00 (DEG) CONT. SCAN RATE : 3.00 DEG/MIN.

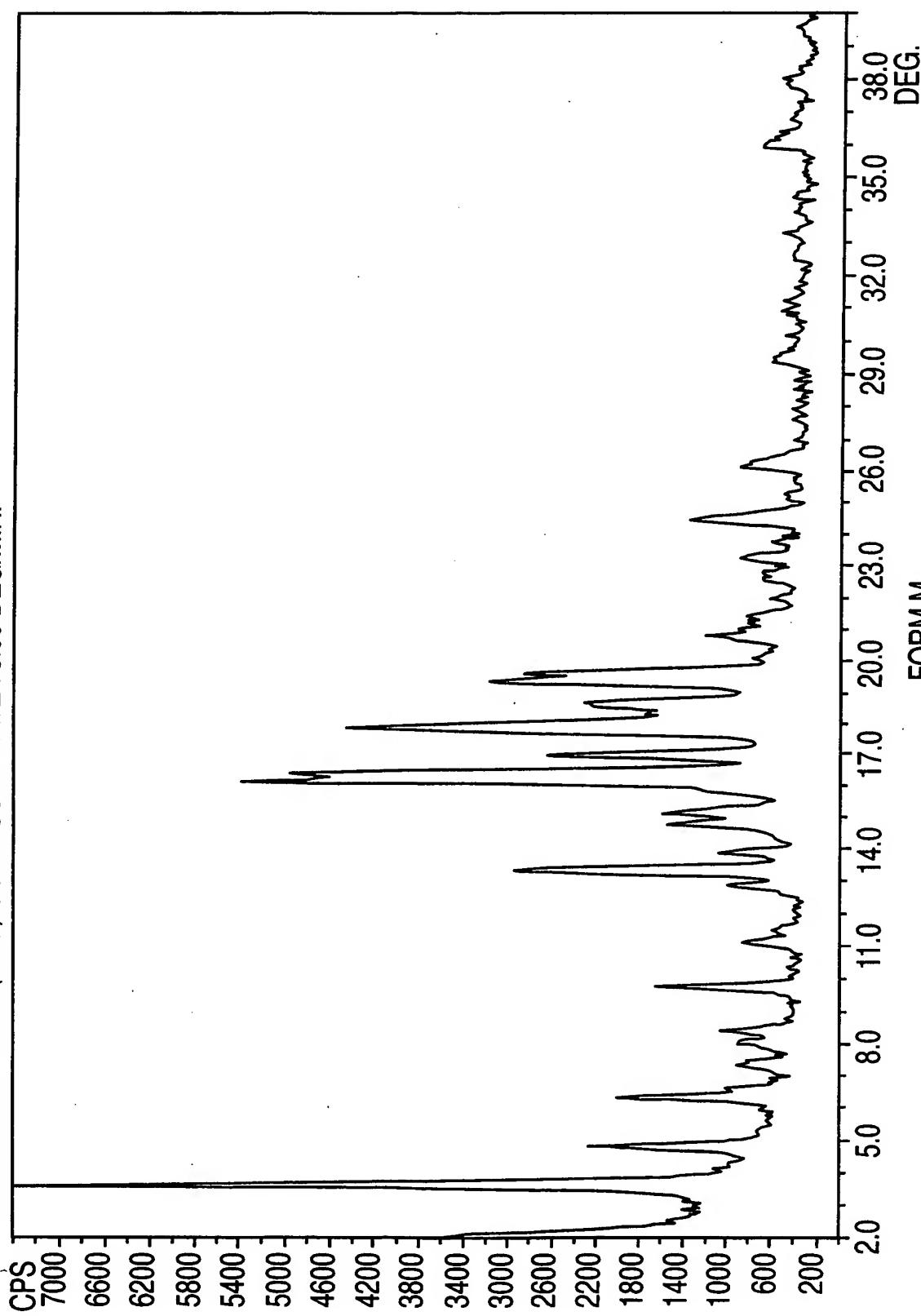
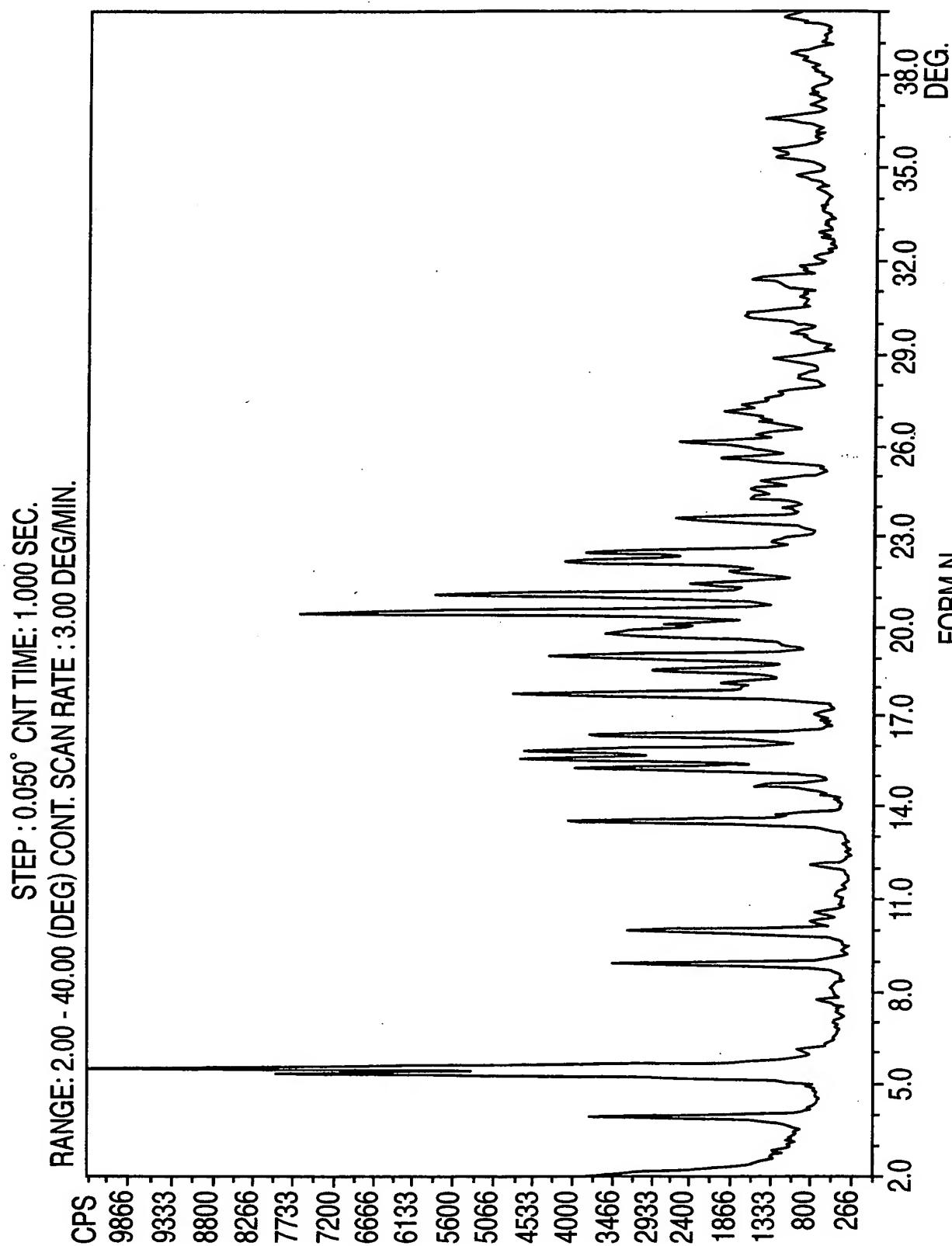


FIG. 11

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⊕



FORM N
FIG. 12

STEP : 0.050° CNT TIME: 1.000 SEC.
RANGE: 2.00 - 40.00 (DEG) CONT. SCAN RATE : 3.00 DEG/MIN.

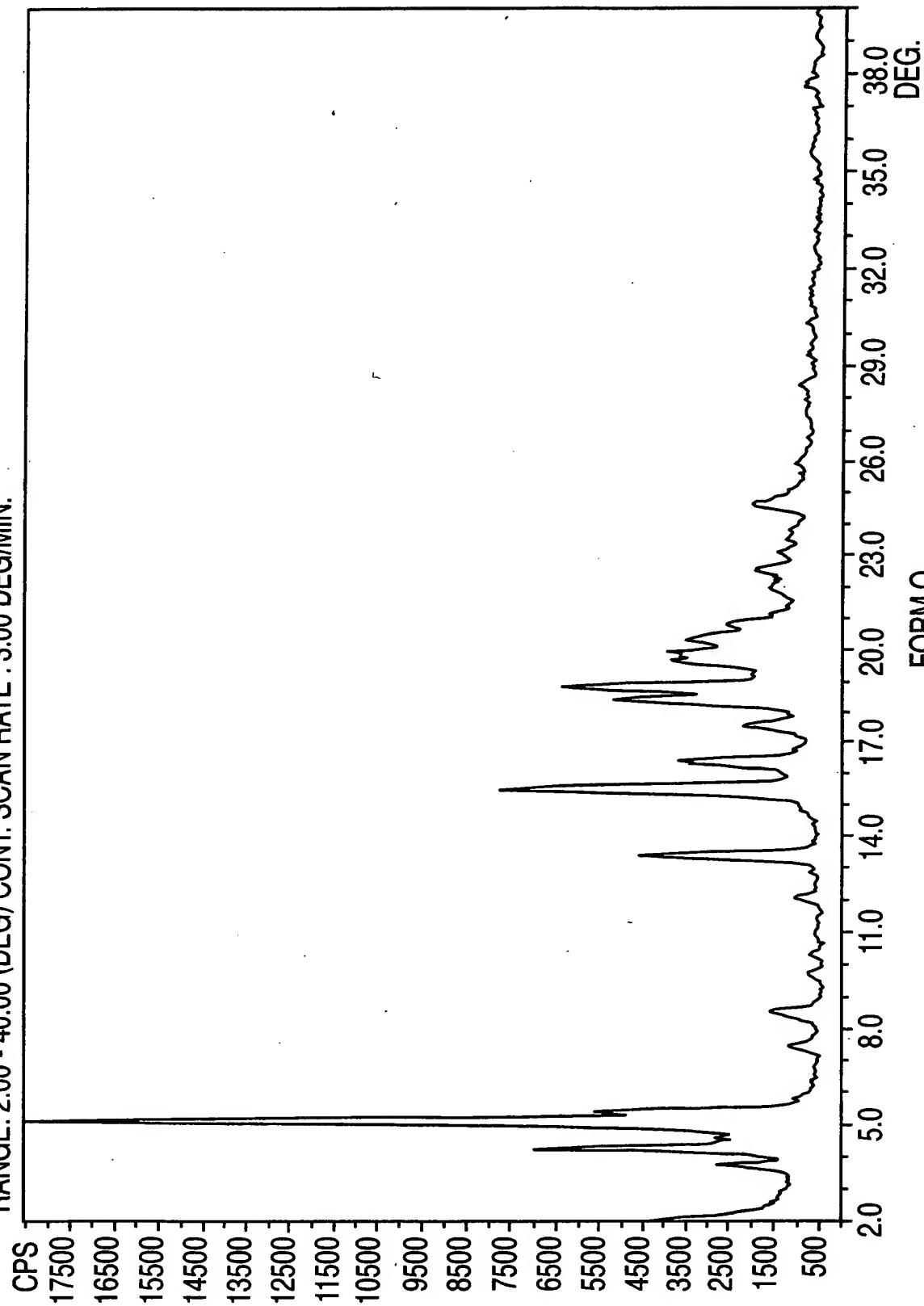


FIG. 13

STEP : 0.050° CNT TIME: 1.000 SEC.
RANGE: 2.00 - 40.00 (DEG) CONT. SCAN RATE : 3.00 DEG/MIN.

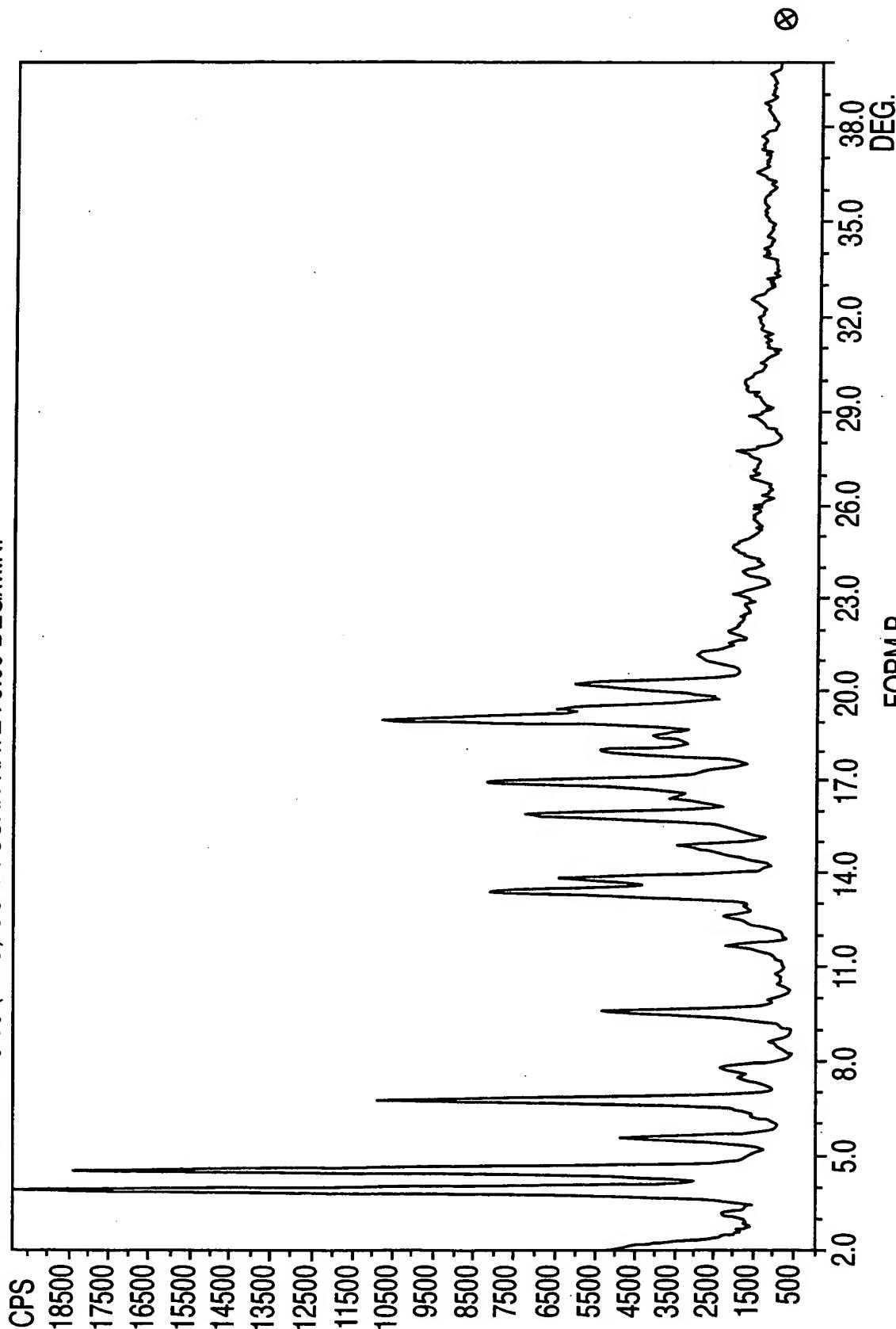


FIG. 14

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STEP : 0.050° CNT TIME: 1.000 SEC.
RANGE: 2.00 - 40.00 (DEG) CONT. SCAN RATE : 3.00 DEG/MIN.

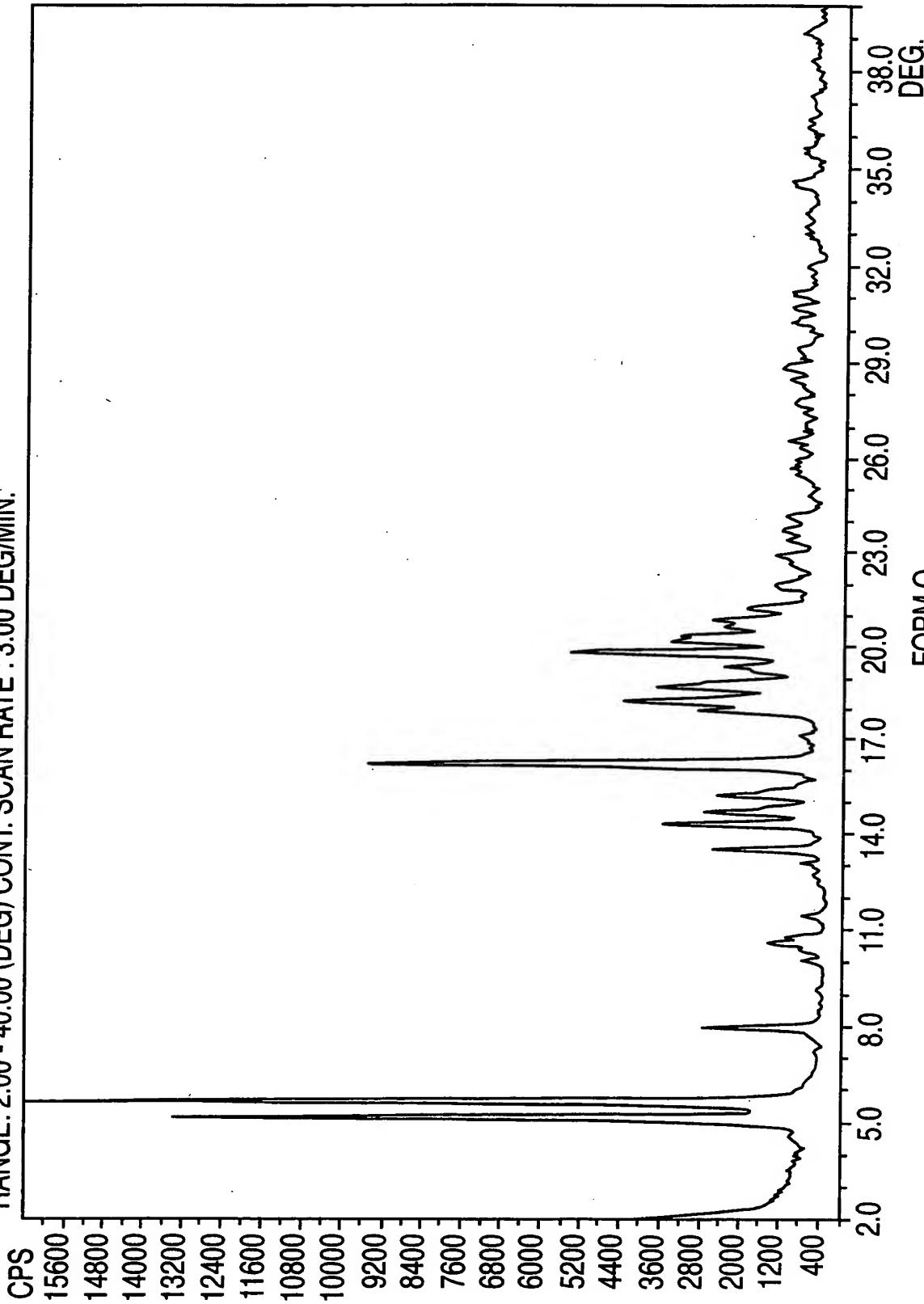


FIG. 15
FORM Q

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STEP : 0.050° CNT TIME: 1.000 SEC.
RANGE: 2.00 - 40.00 (DEG) CONT. SCAN RATE : 3.00 DEG/MIN.

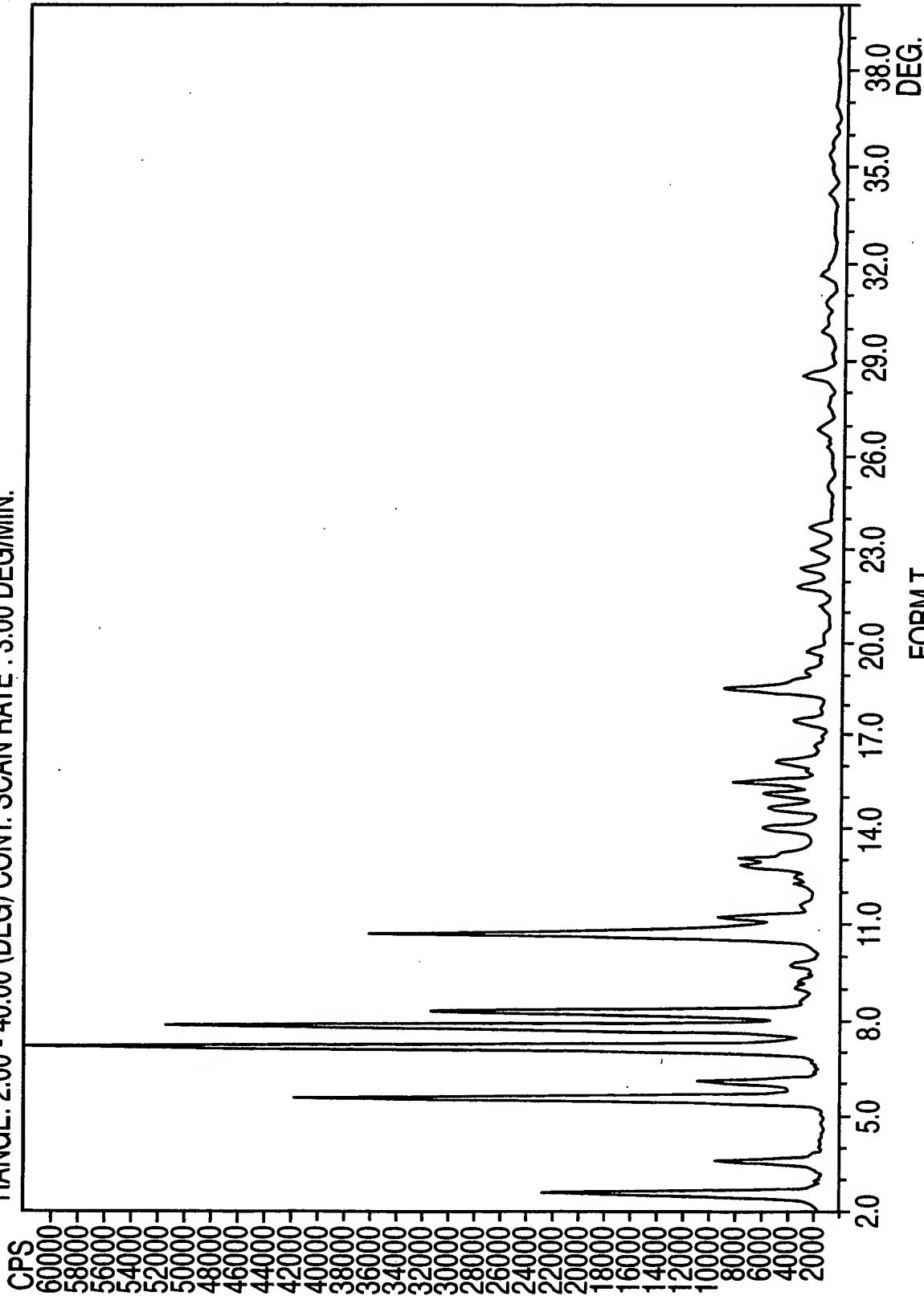


FIG. 16

STEP : 0.050° CNT TIME: 1.000 SEC.
RANGE: 2.00 - 40.00 (DEG) CONT. SCAN RATE : 3.00 DEG/MIN.

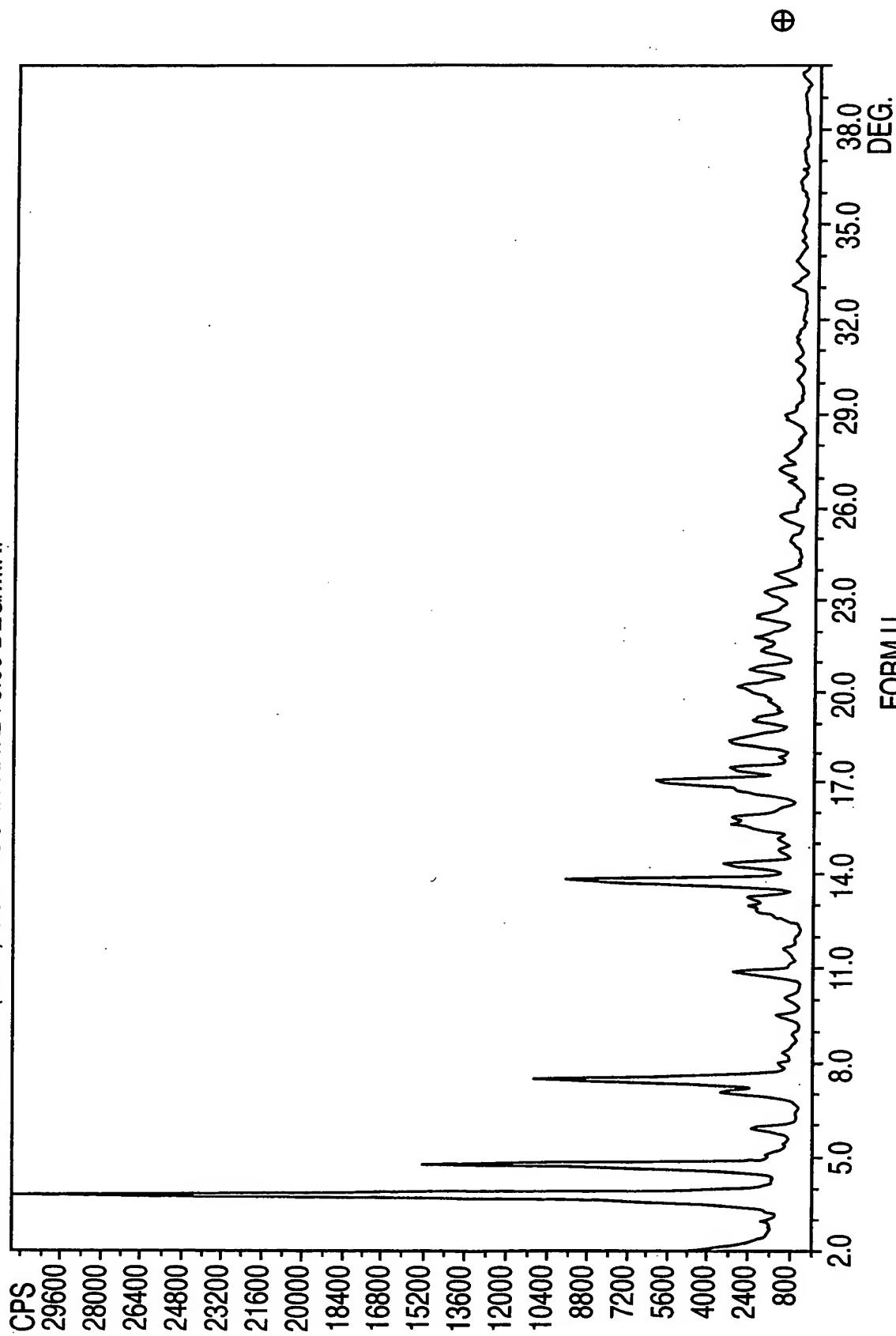


FIG. 17

⊕

STEP : 0.050° CNT TIME: 1.000 SEC.
RANGE: 2.00 - 40.00 (DEG) CONT. SCAN RATE : 3.00 DEG/MIN.

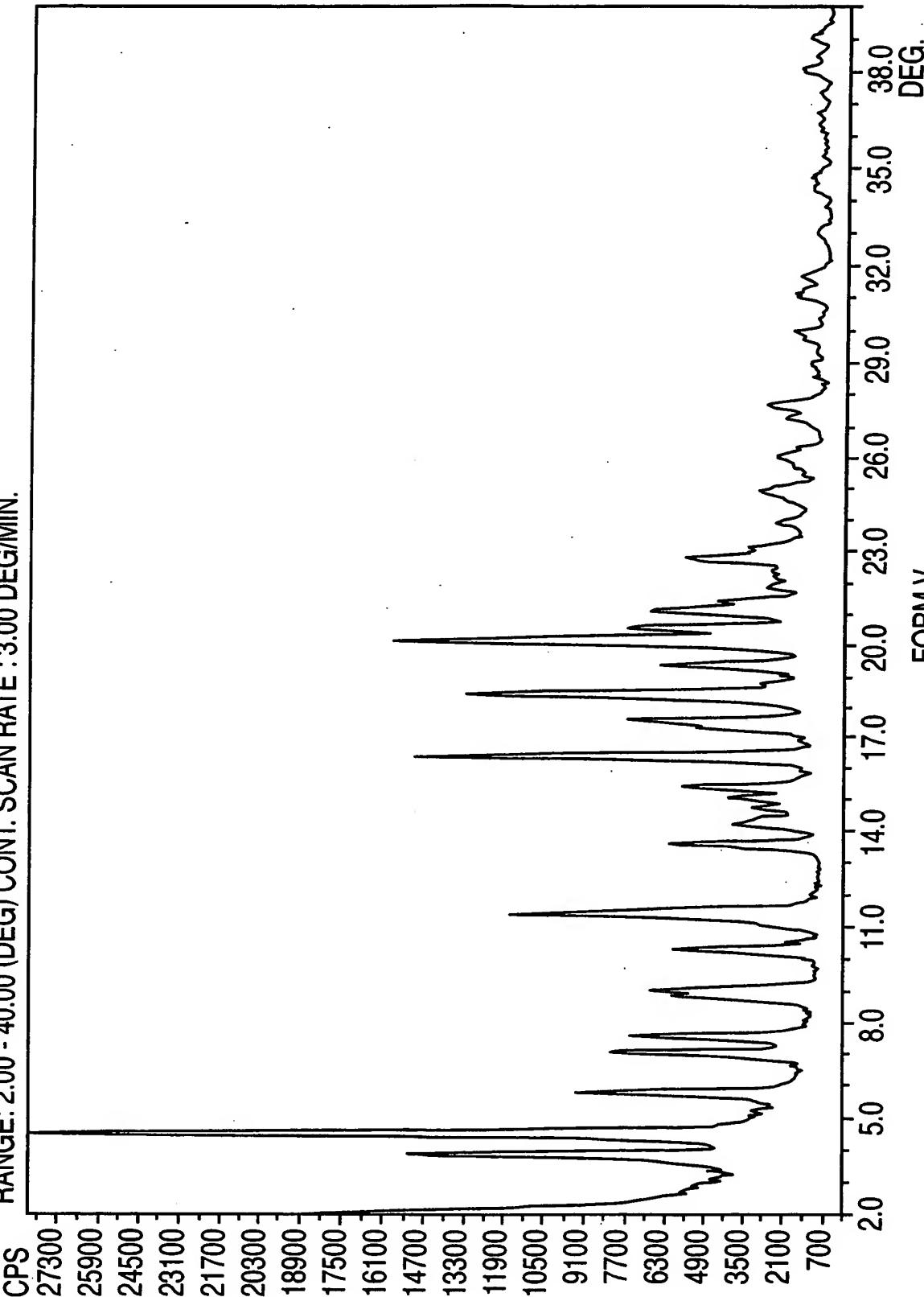
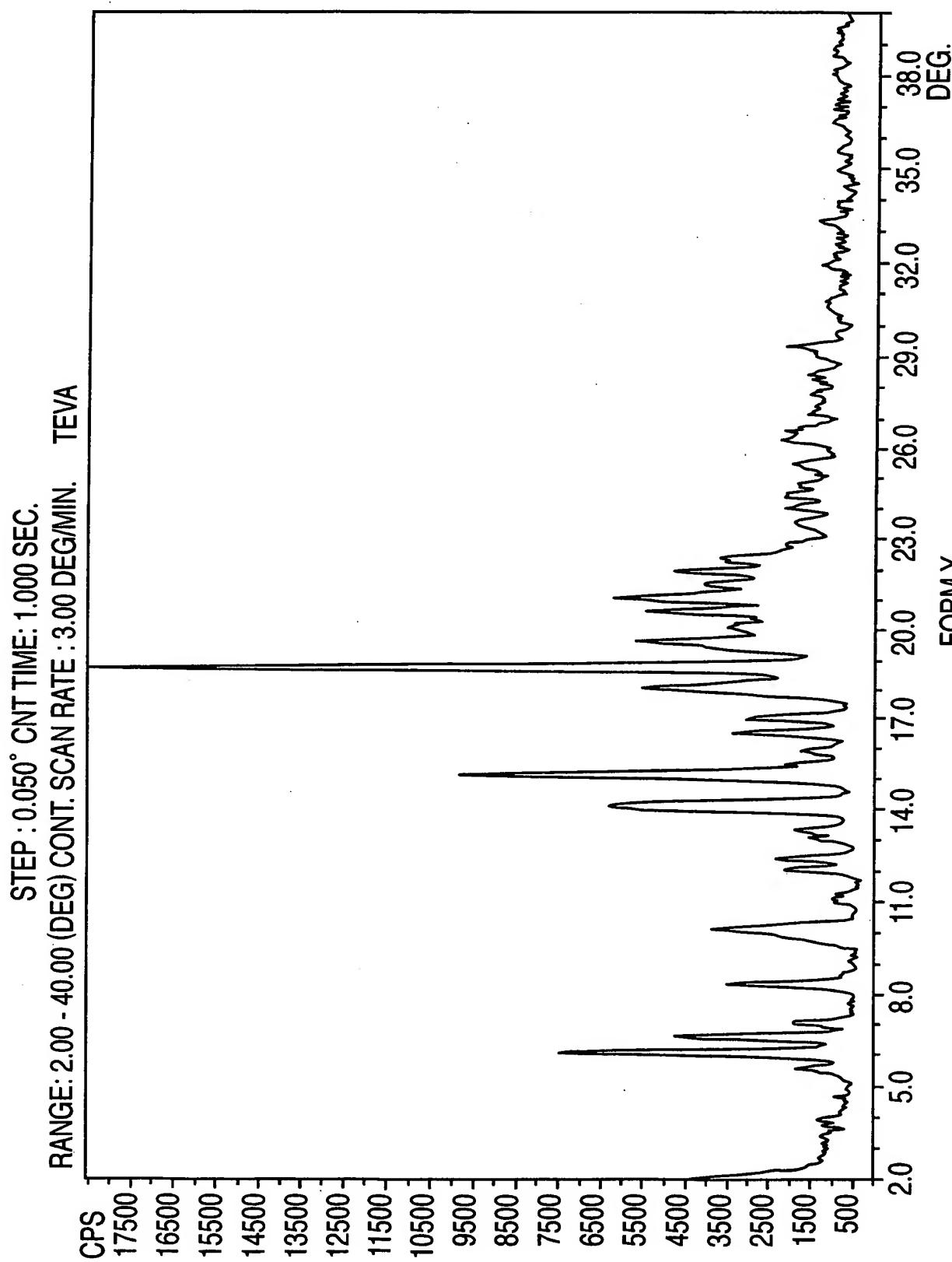
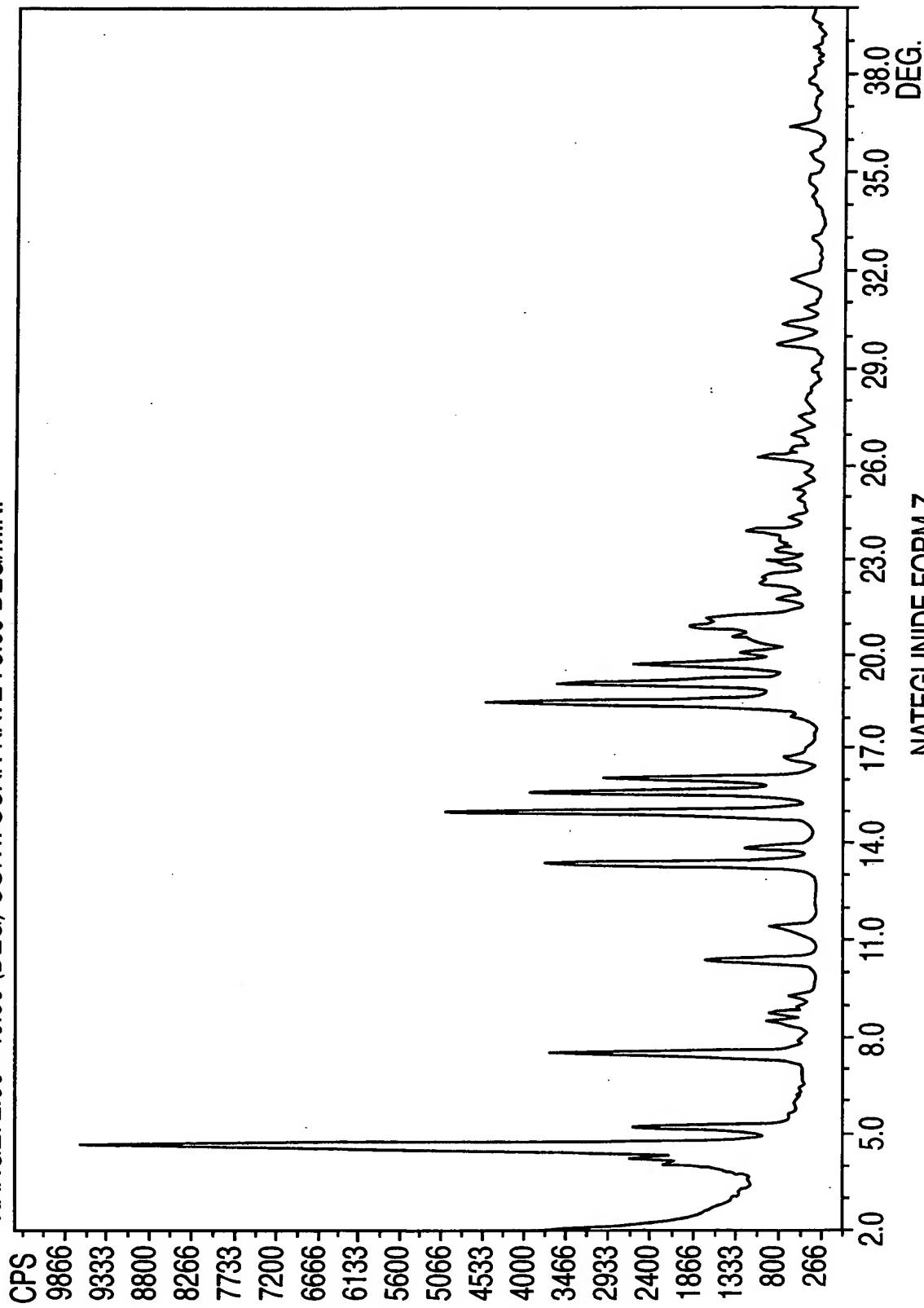


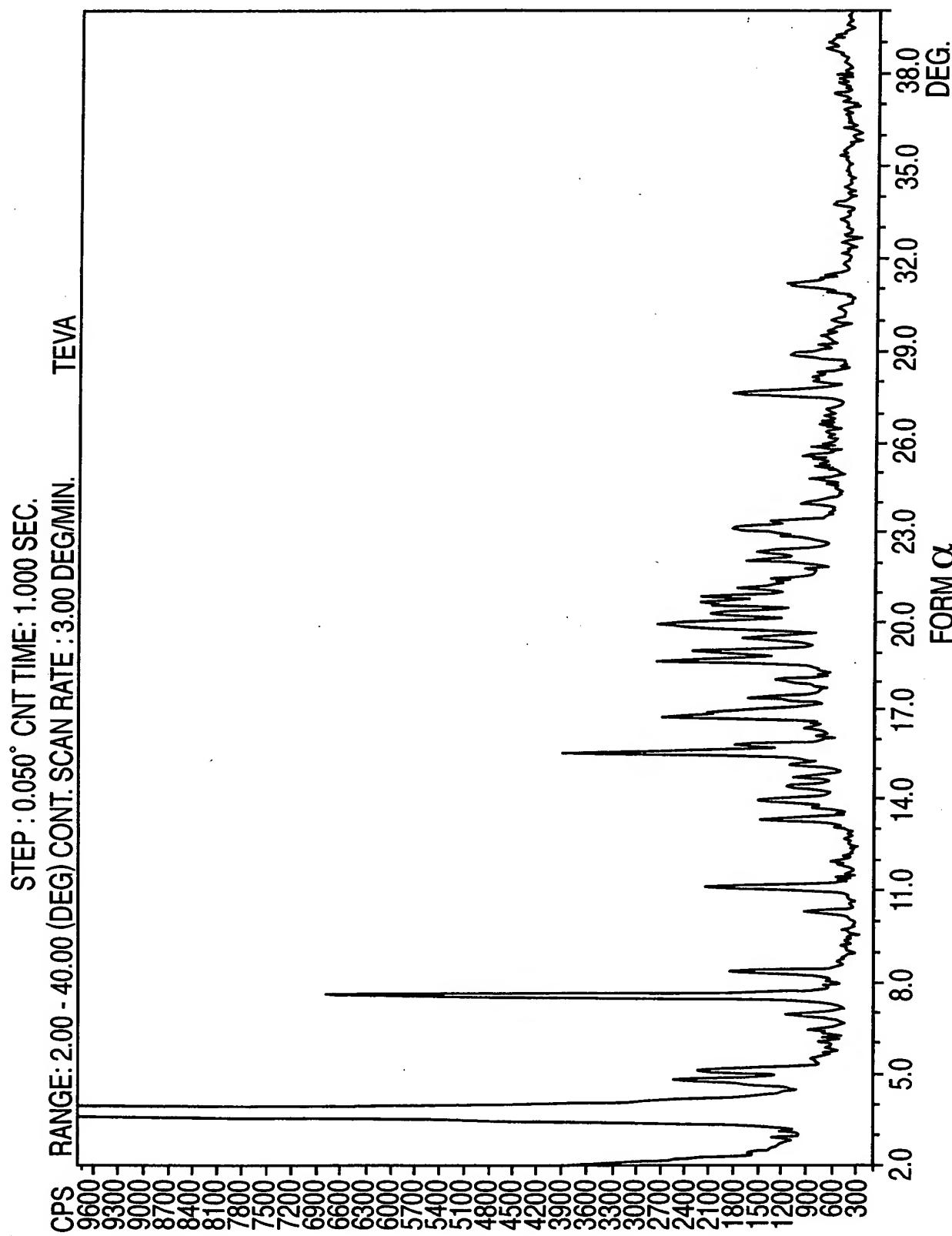
FIG. 18



STEP : 0.050° CNT TIME: 1.000 SEC.
RANGE: 2.00 - 40.00 (DEG) CONT. SCAN RATE : 3.00 DEG/MIN.



NATEGLINIDE FORM Z
FIG. 20



STEP : 0.050° CNT TIME: 1.000 SEC.
RANGE: 2.00 - 40.00 (DEG) CONT. SCAN RATE : 3.00 DEG/MIN. TEVA

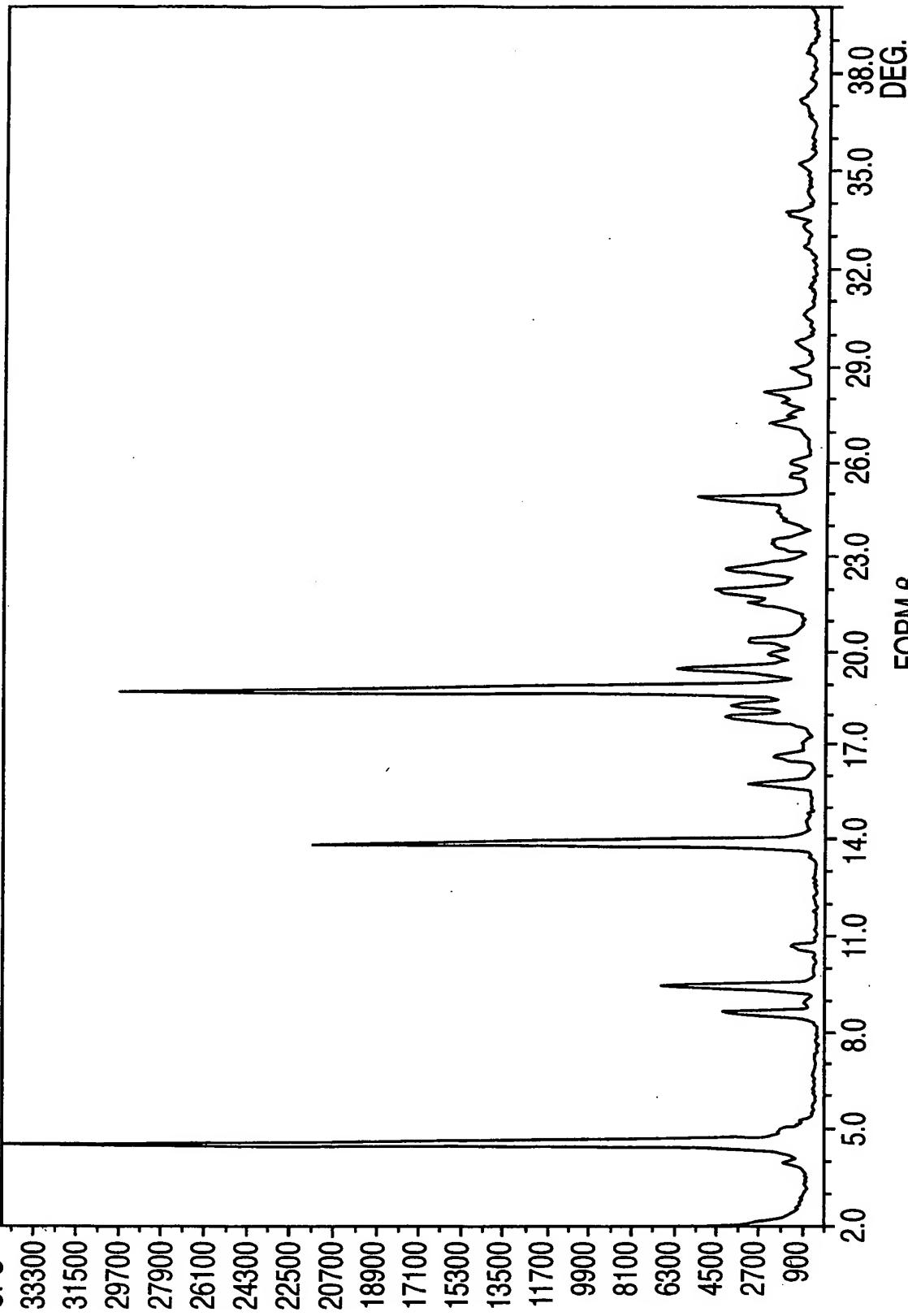


FIG. 22
FORM β

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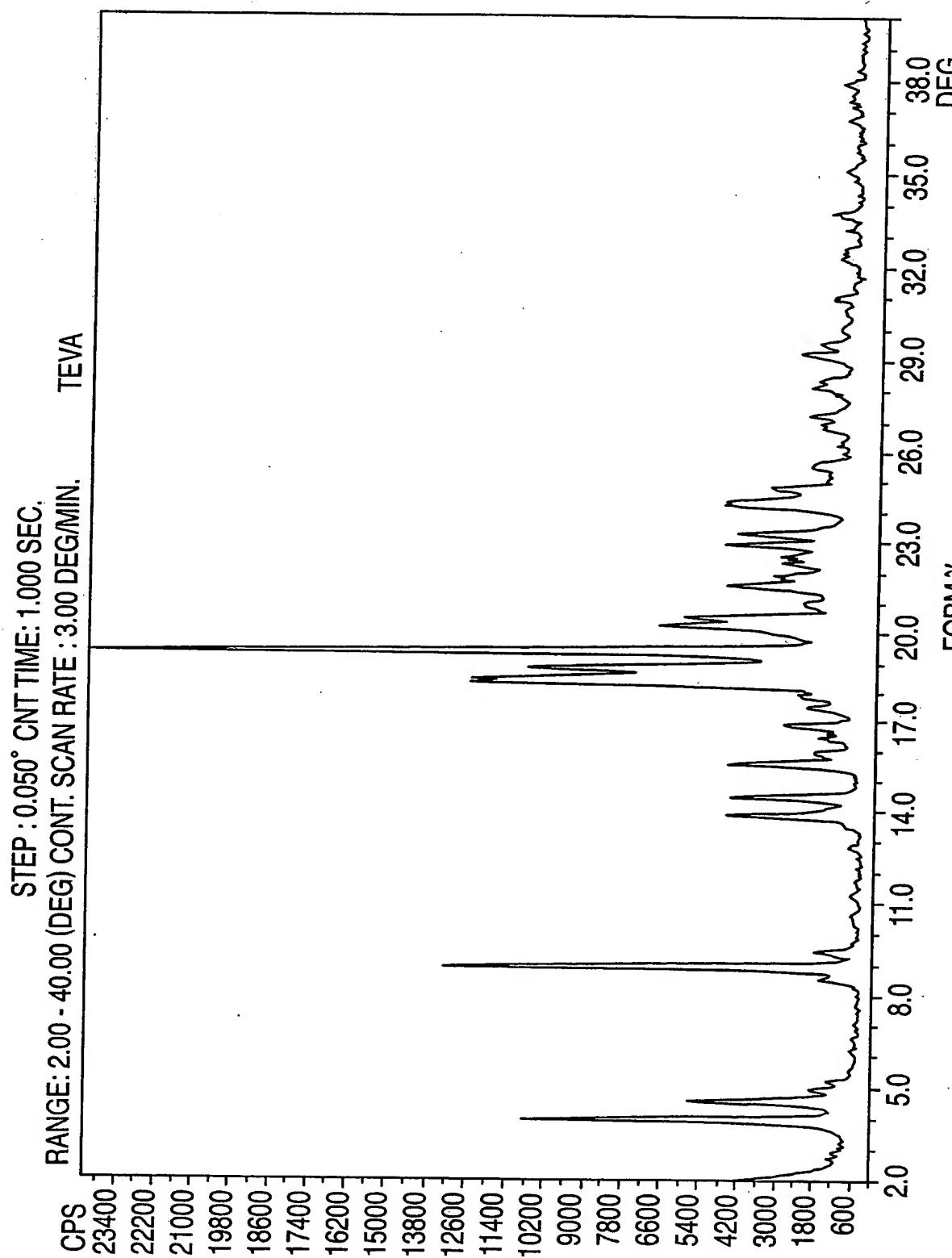


FIG. 23

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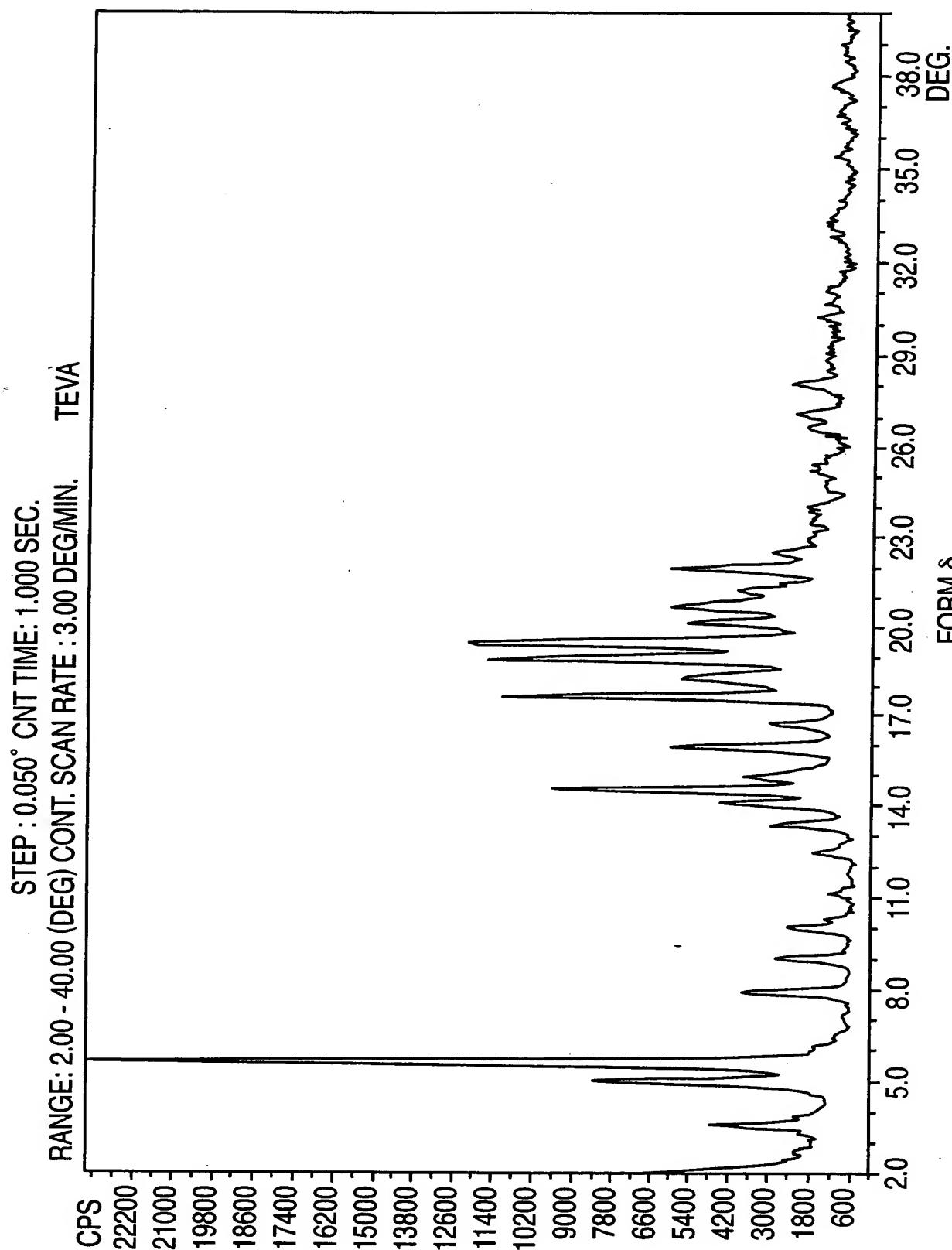
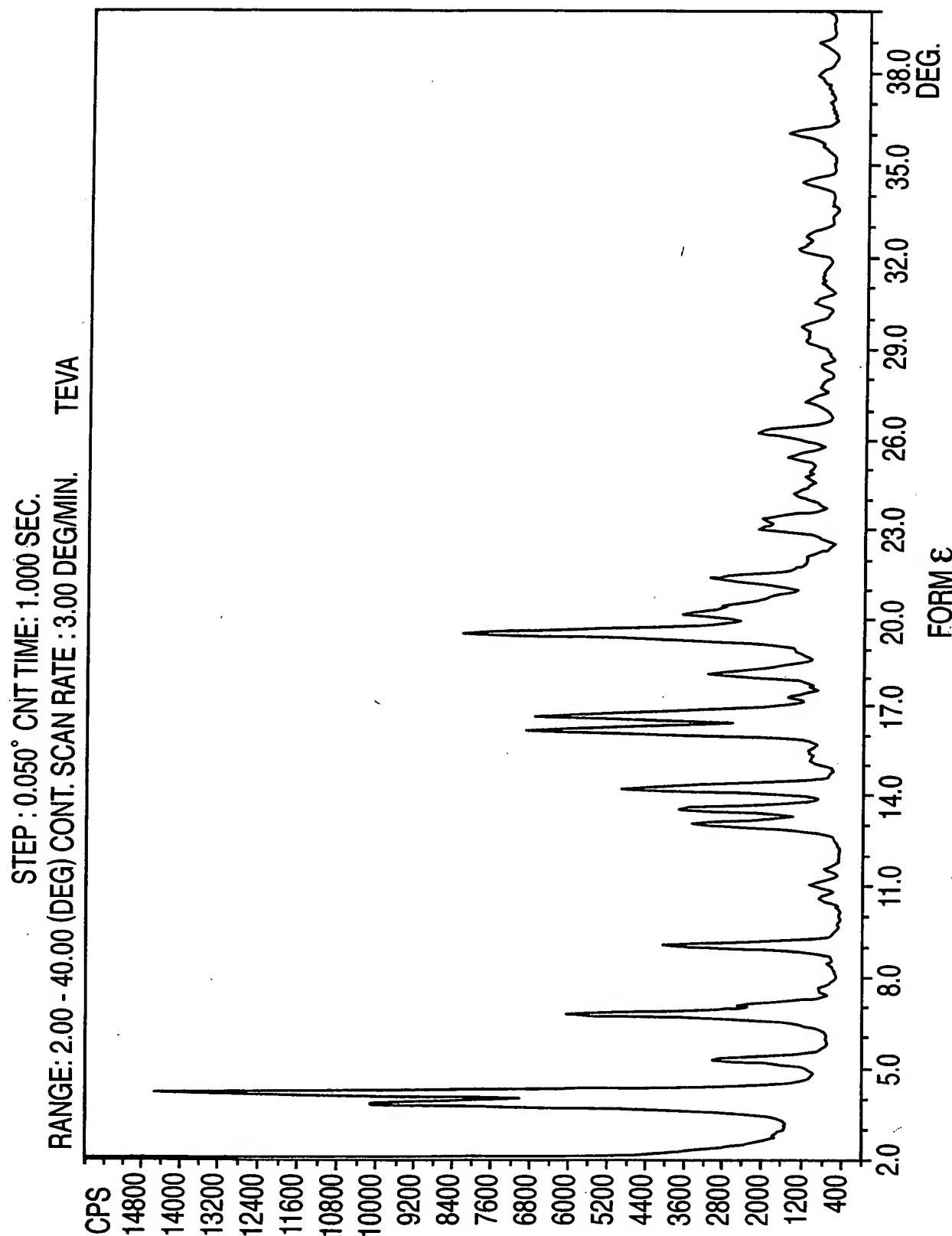
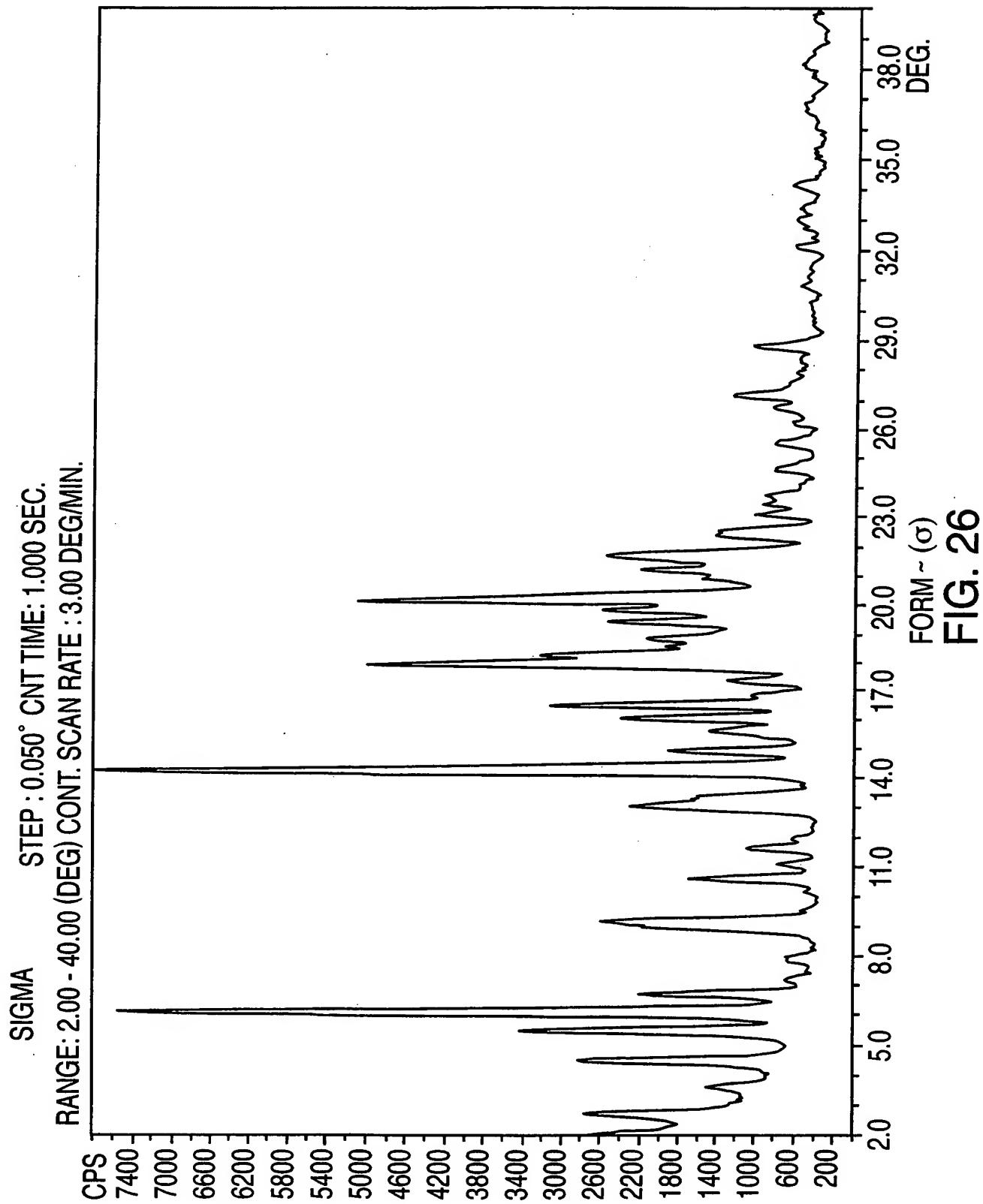
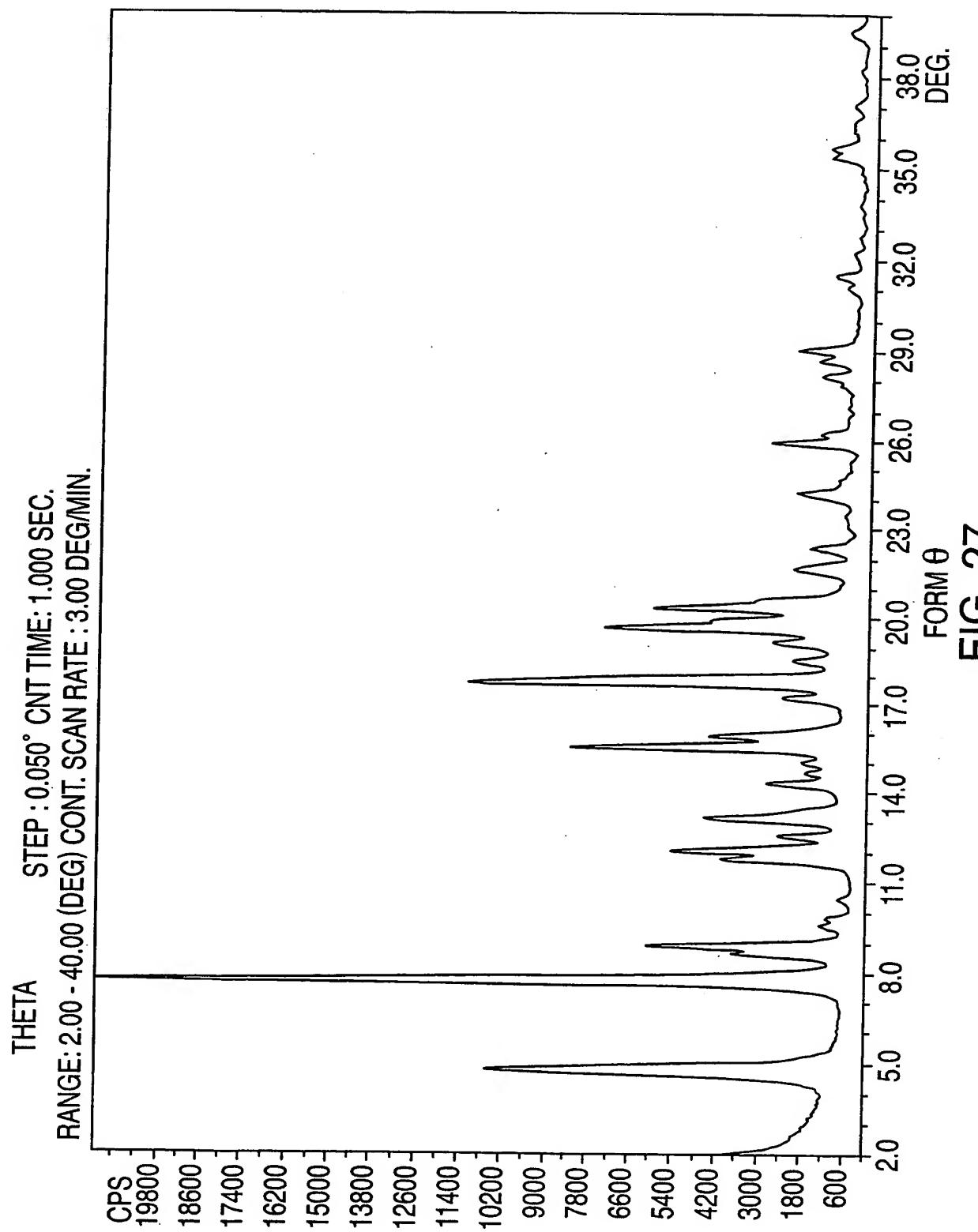


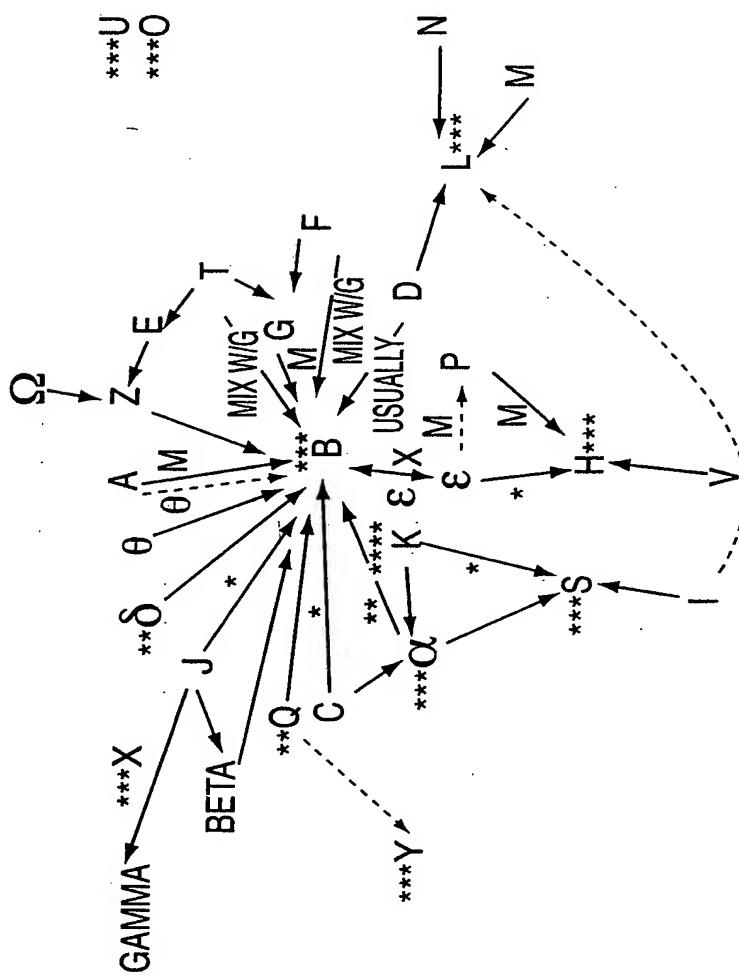
FIG. 24





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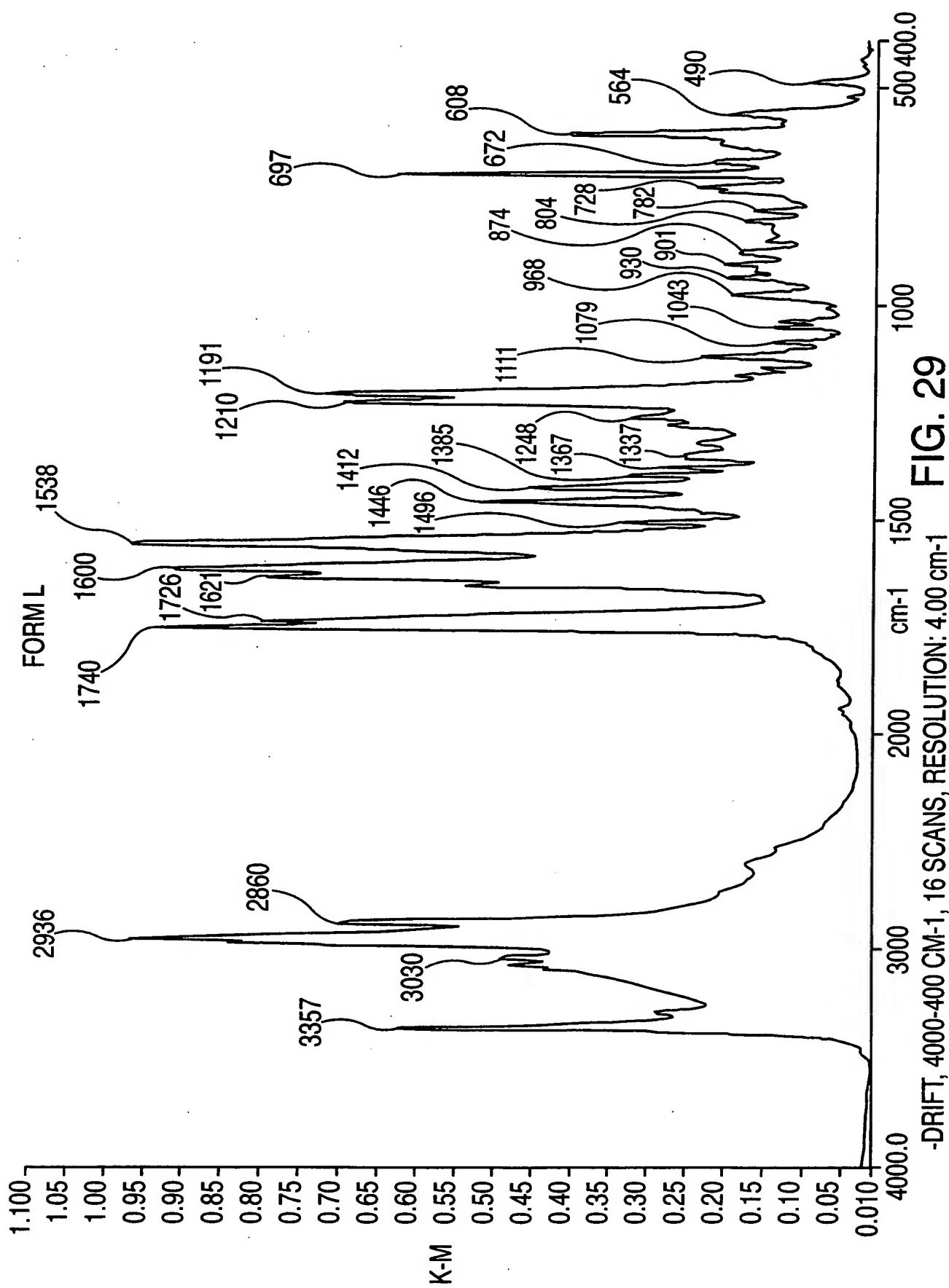


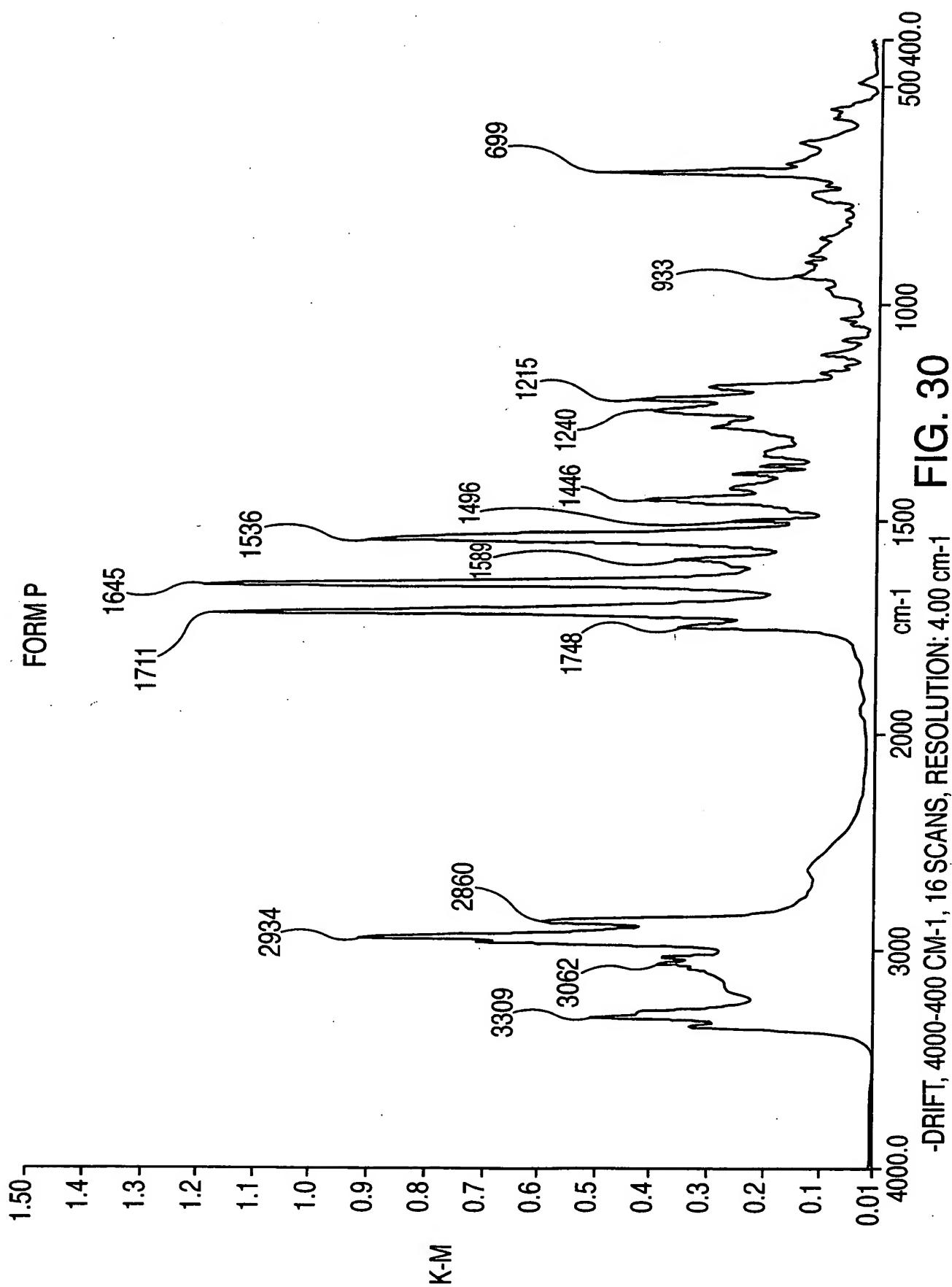
- * TRANSFORMATION MAY PROCEED THROUGH ANOTHER TERM.
- ** THERMALLY STABLE AT LOWER HEATING TEMPERATURES (~50°C).
- *** THERMALLY STABLE FORMS.
- > TRANSFORMATION AFTER STORAGE AT ROOM TEMPERATURE.
- m MIXTURE WITH STARTING FORM.
- ***** WHEN STARTING MATERIAL CONTAINS SEEDS.
- so RESULTS MIGHT VARY DEPENDING ON THE SOLVATE OF FORM EP.

THERMAL STABILITY CHART

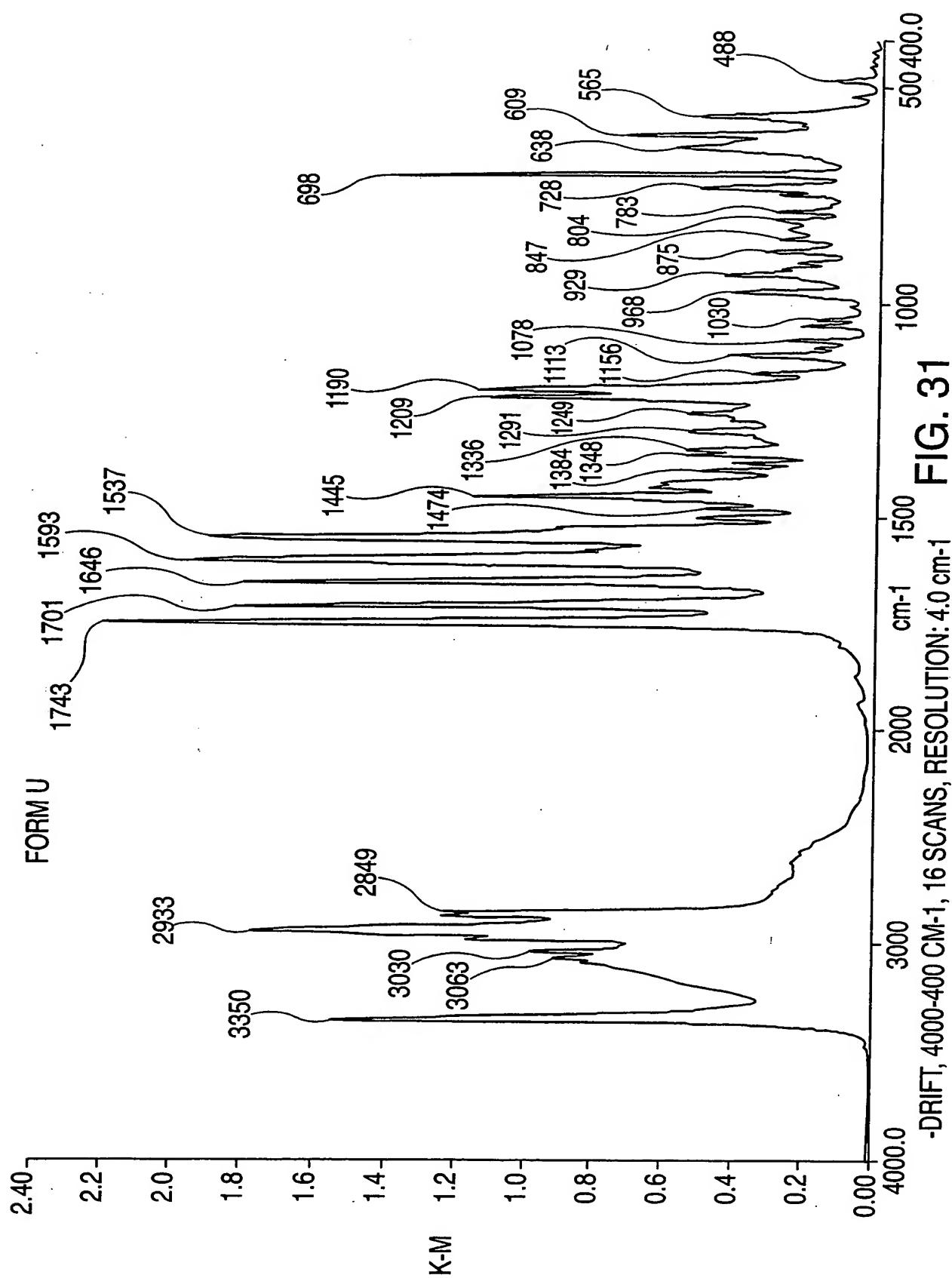
FIG. 28

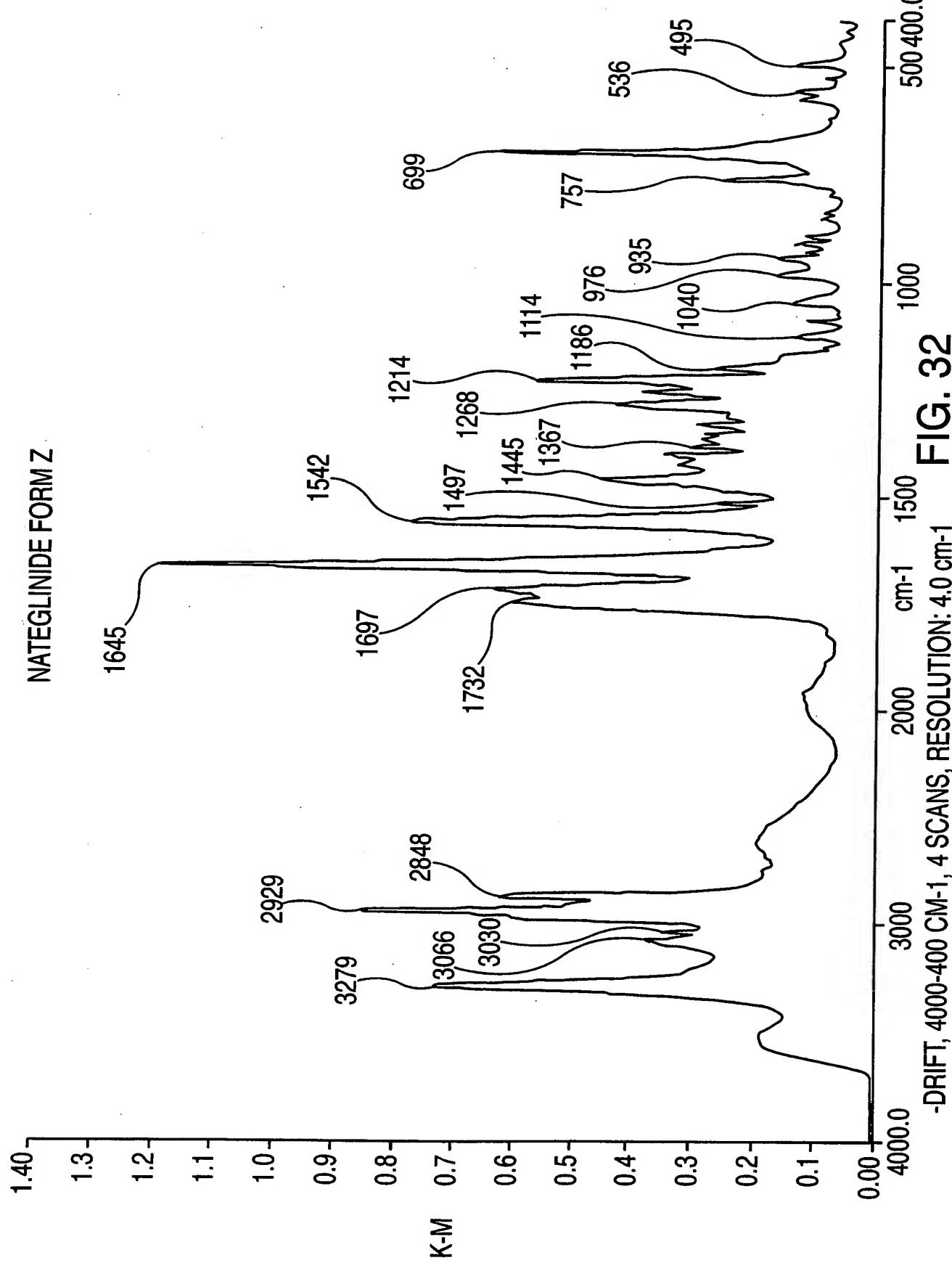
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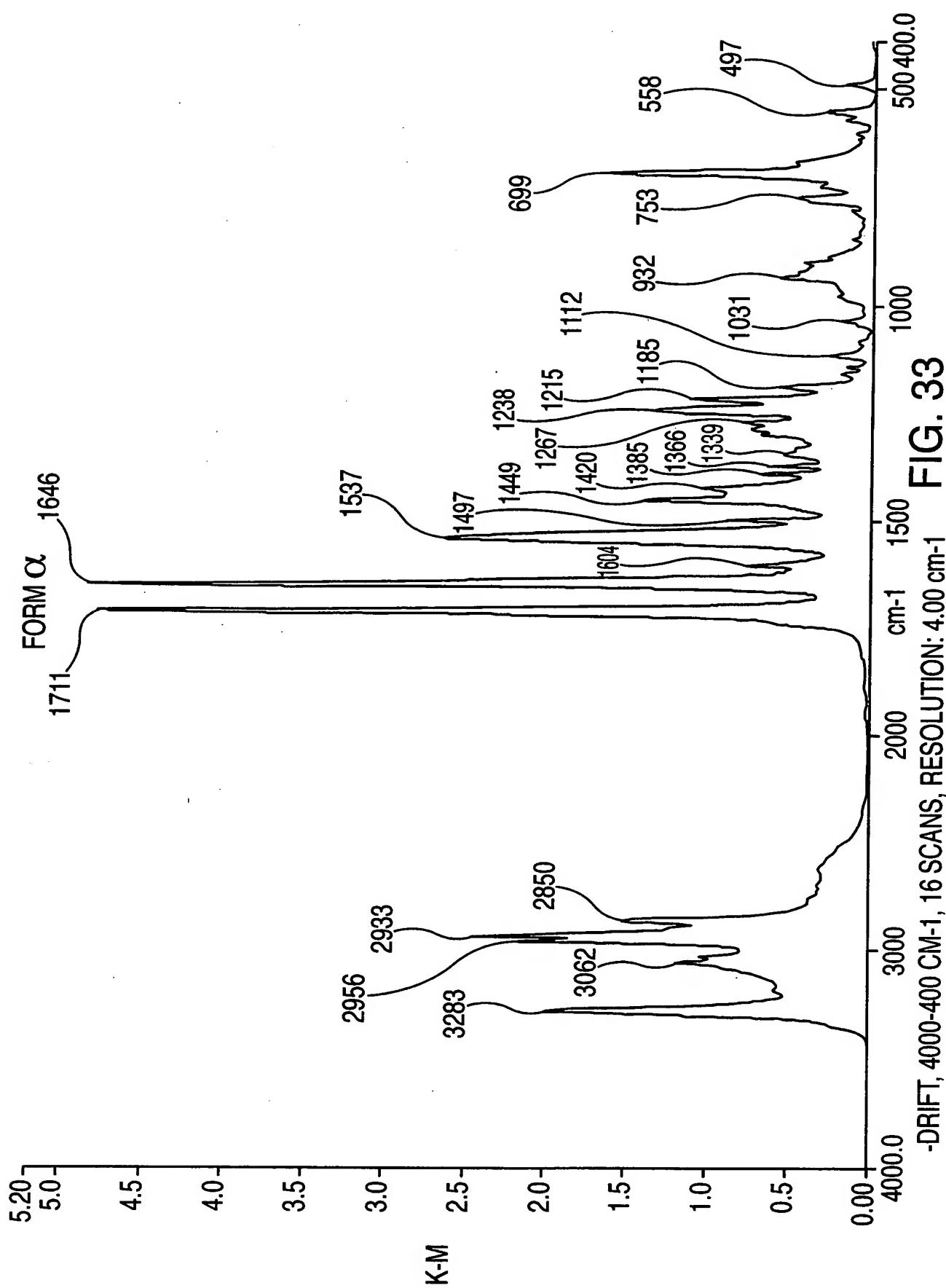


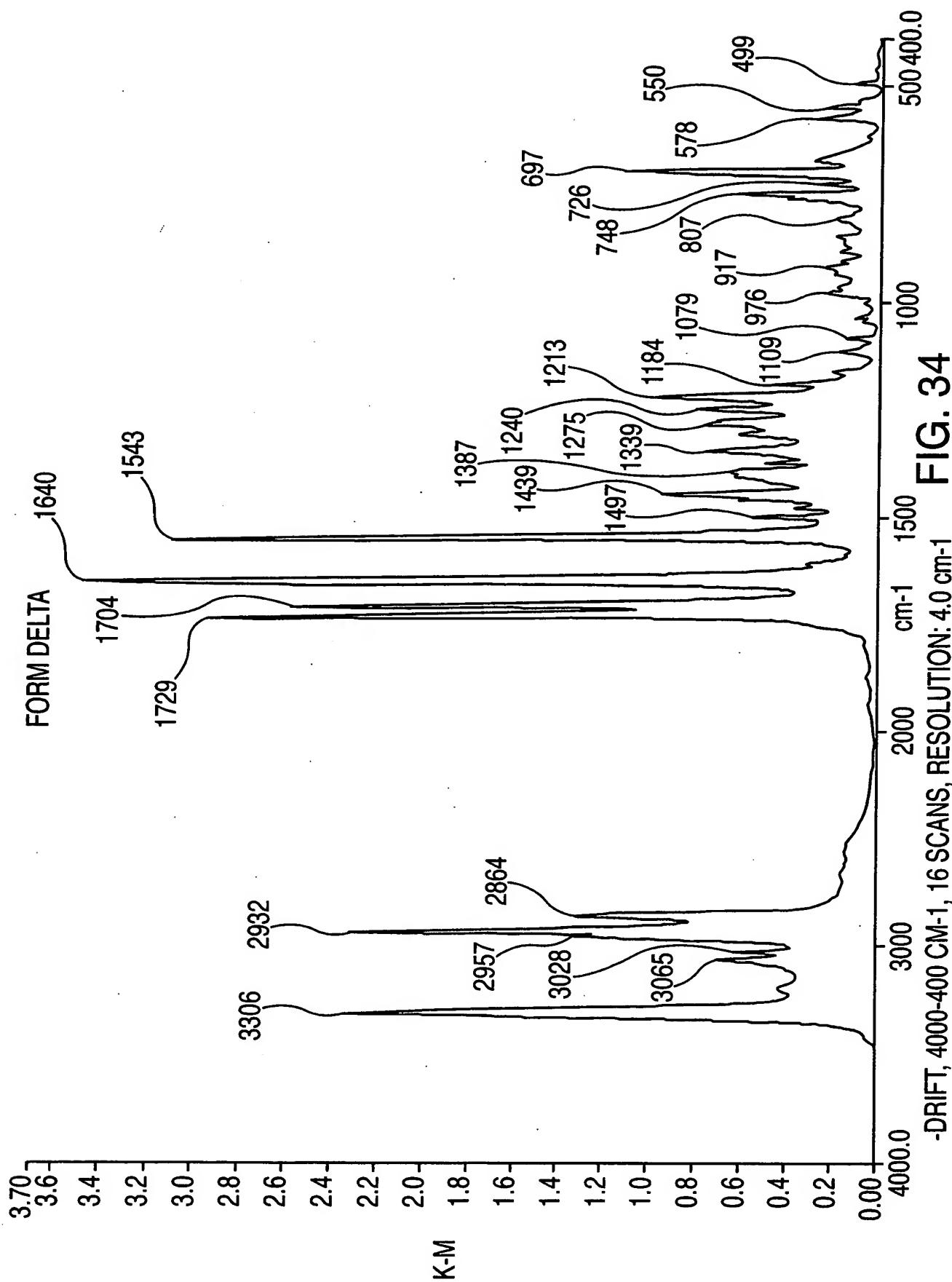


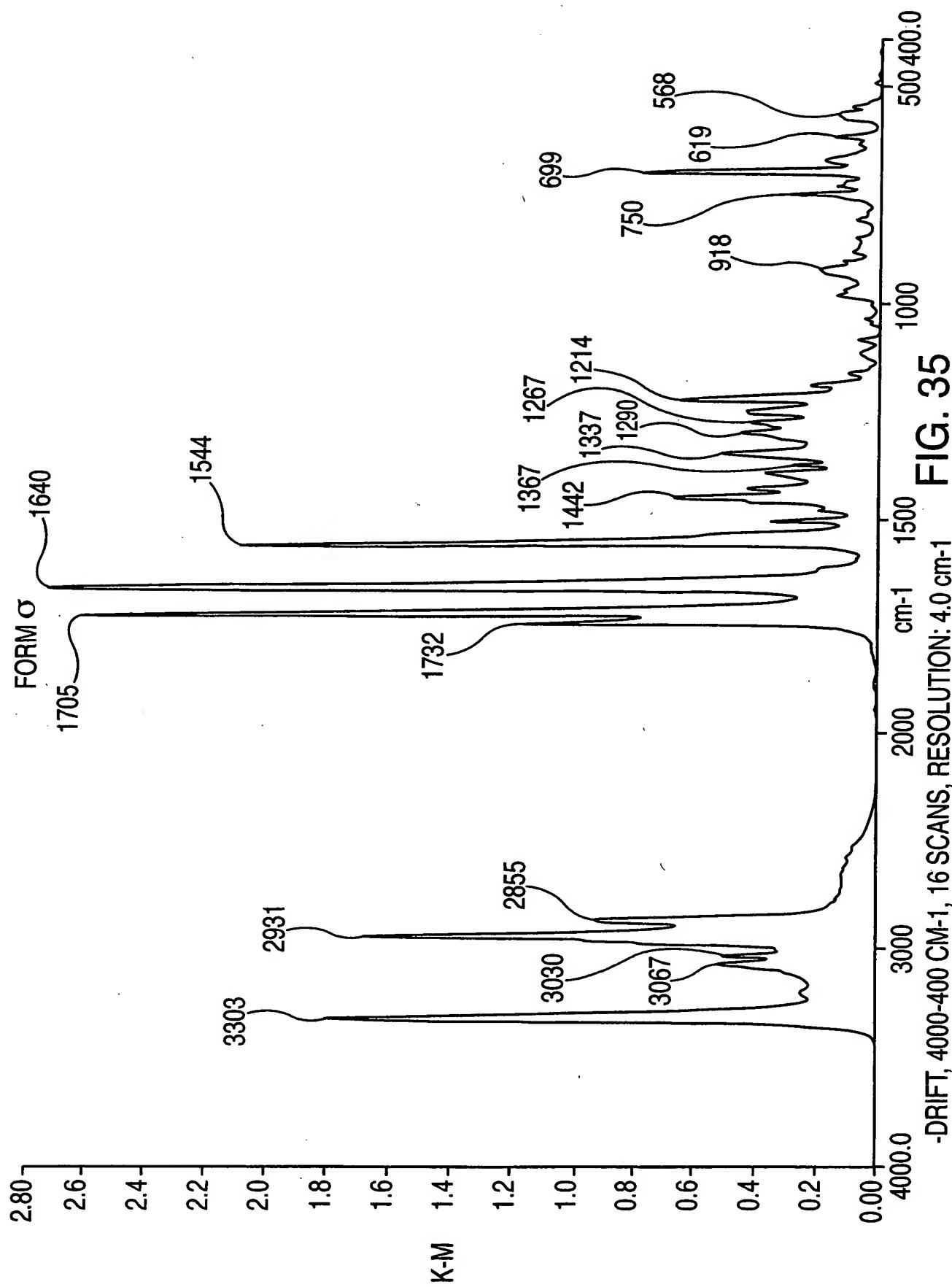
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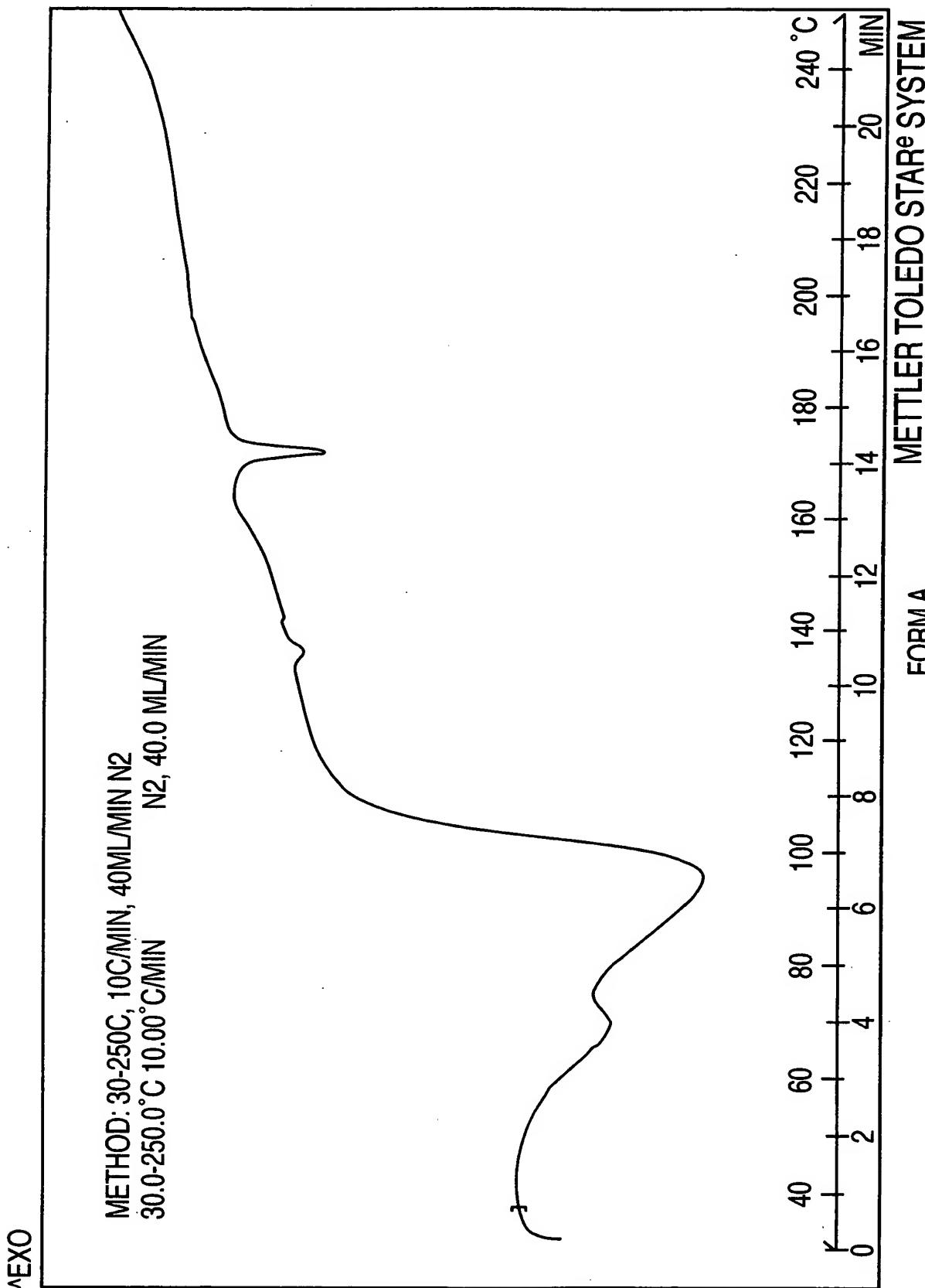
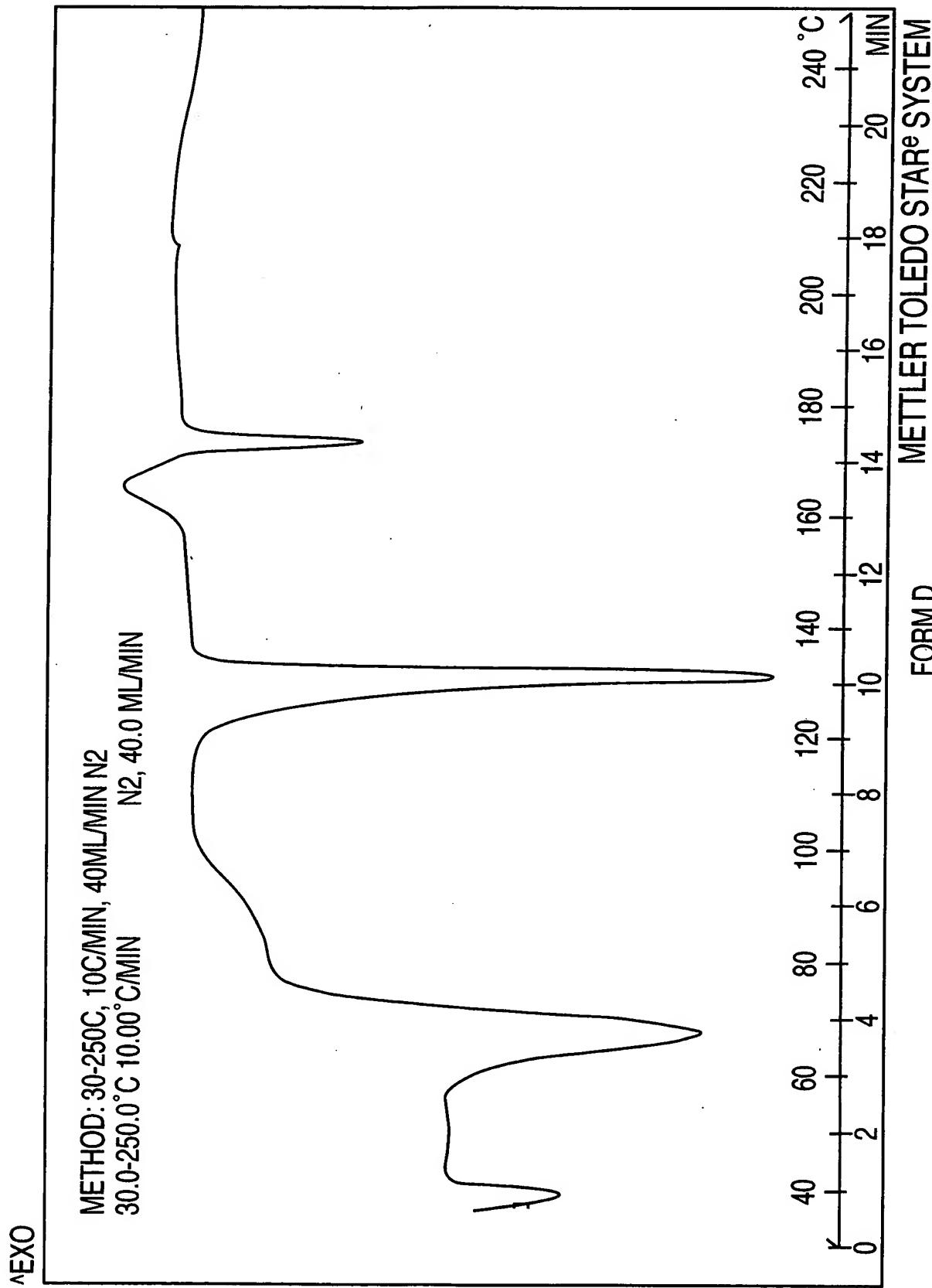
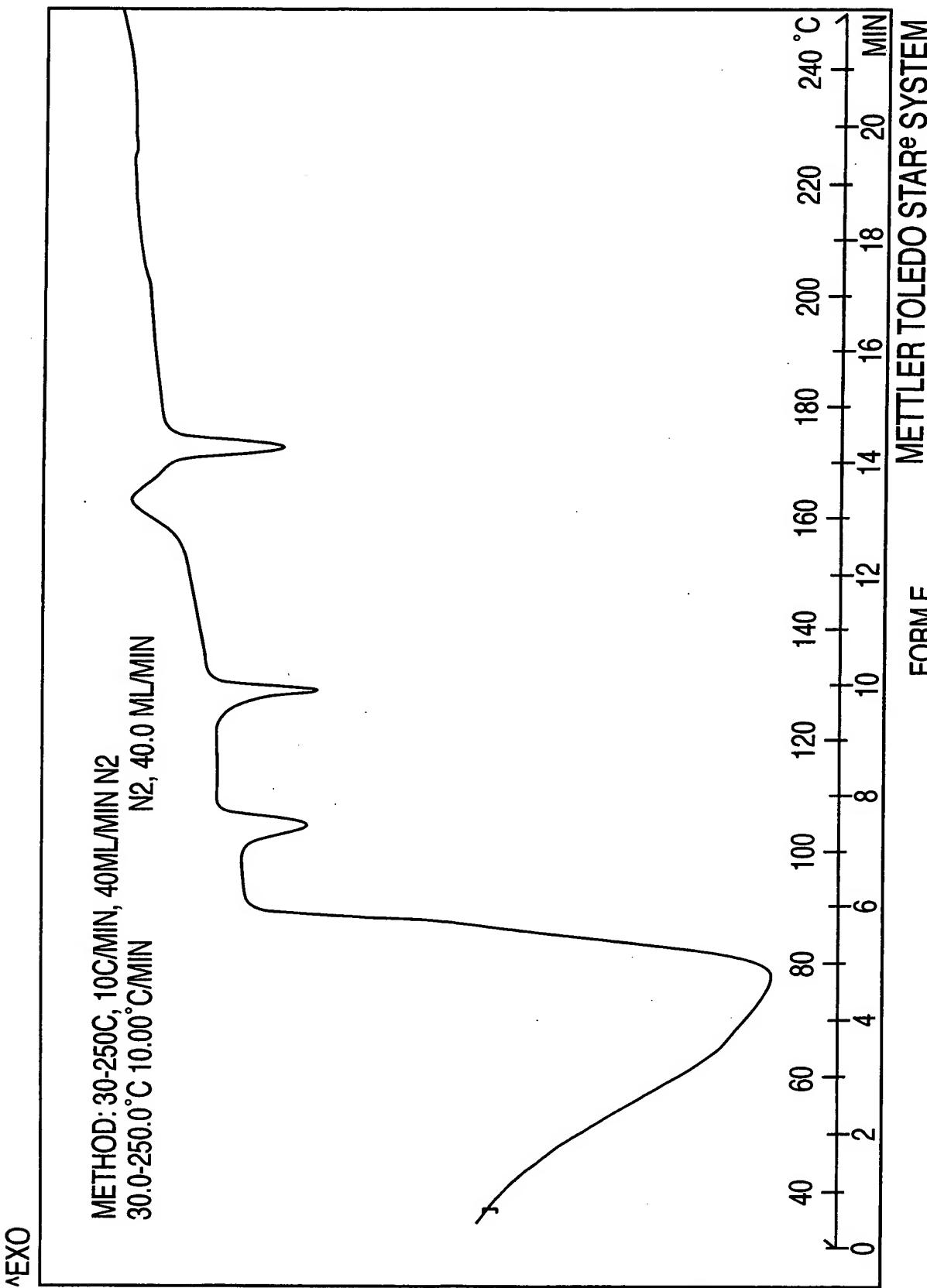


FIG. 36



FORM D
FIG. 37



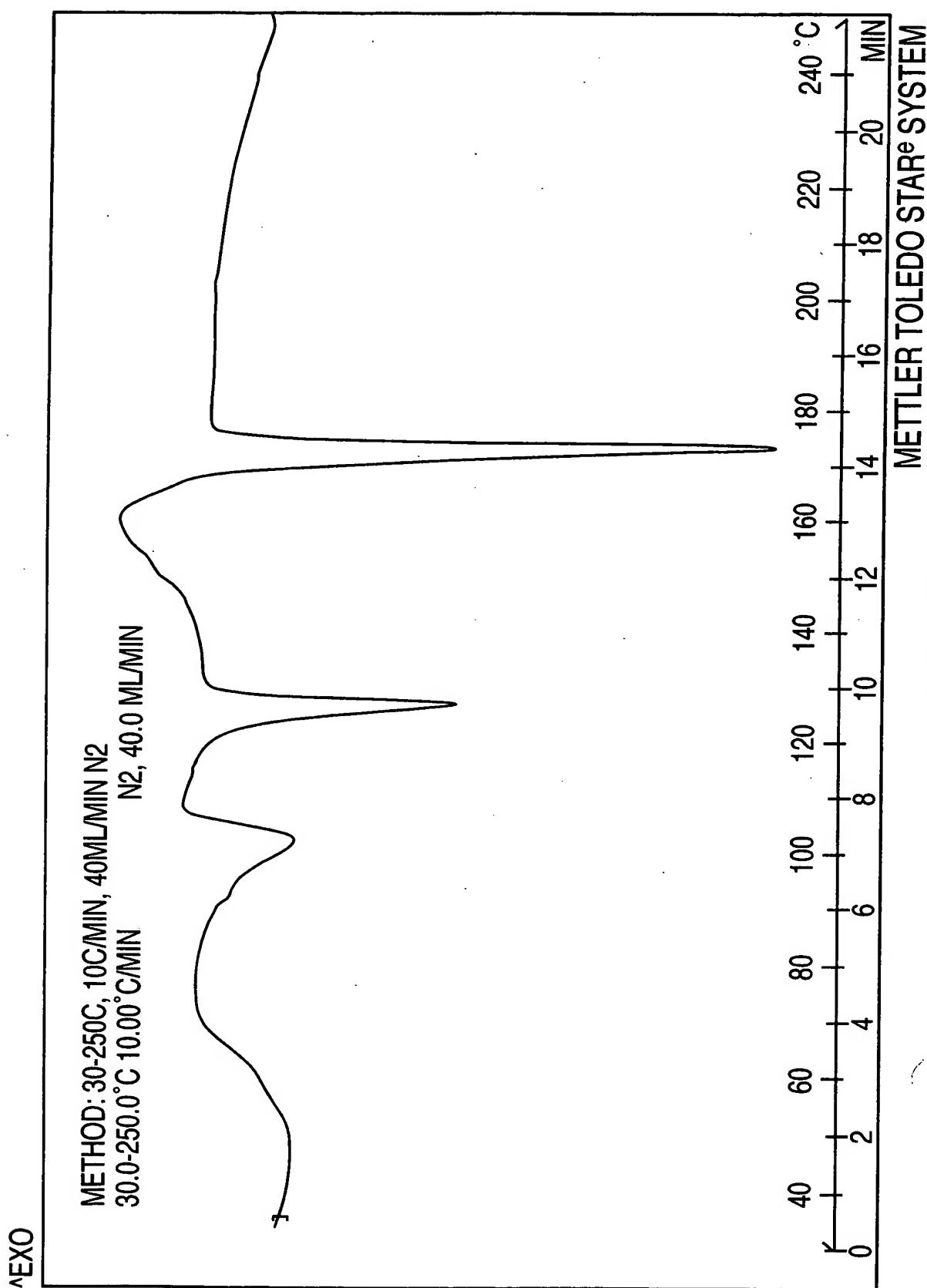


FIG. 39

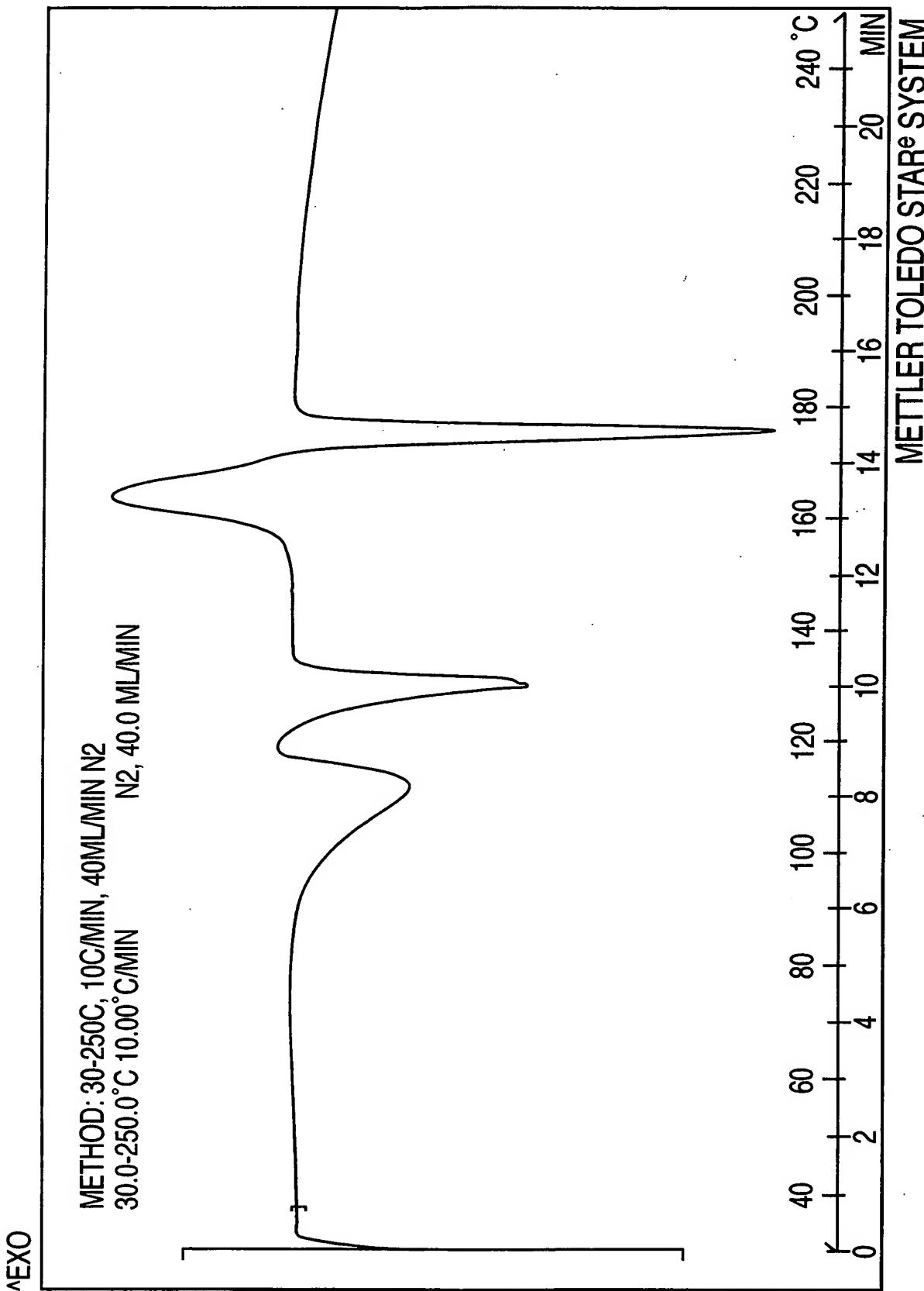
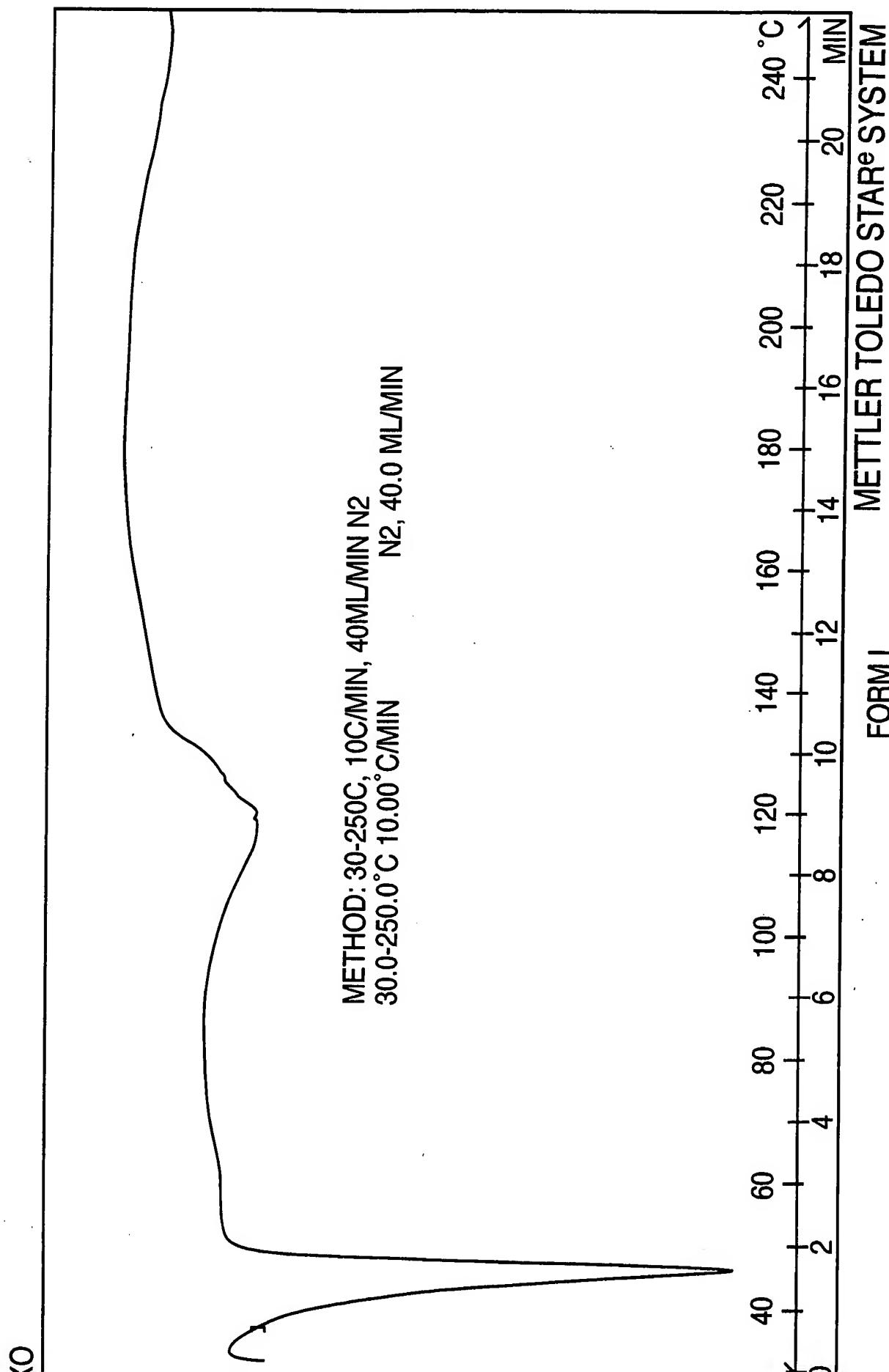
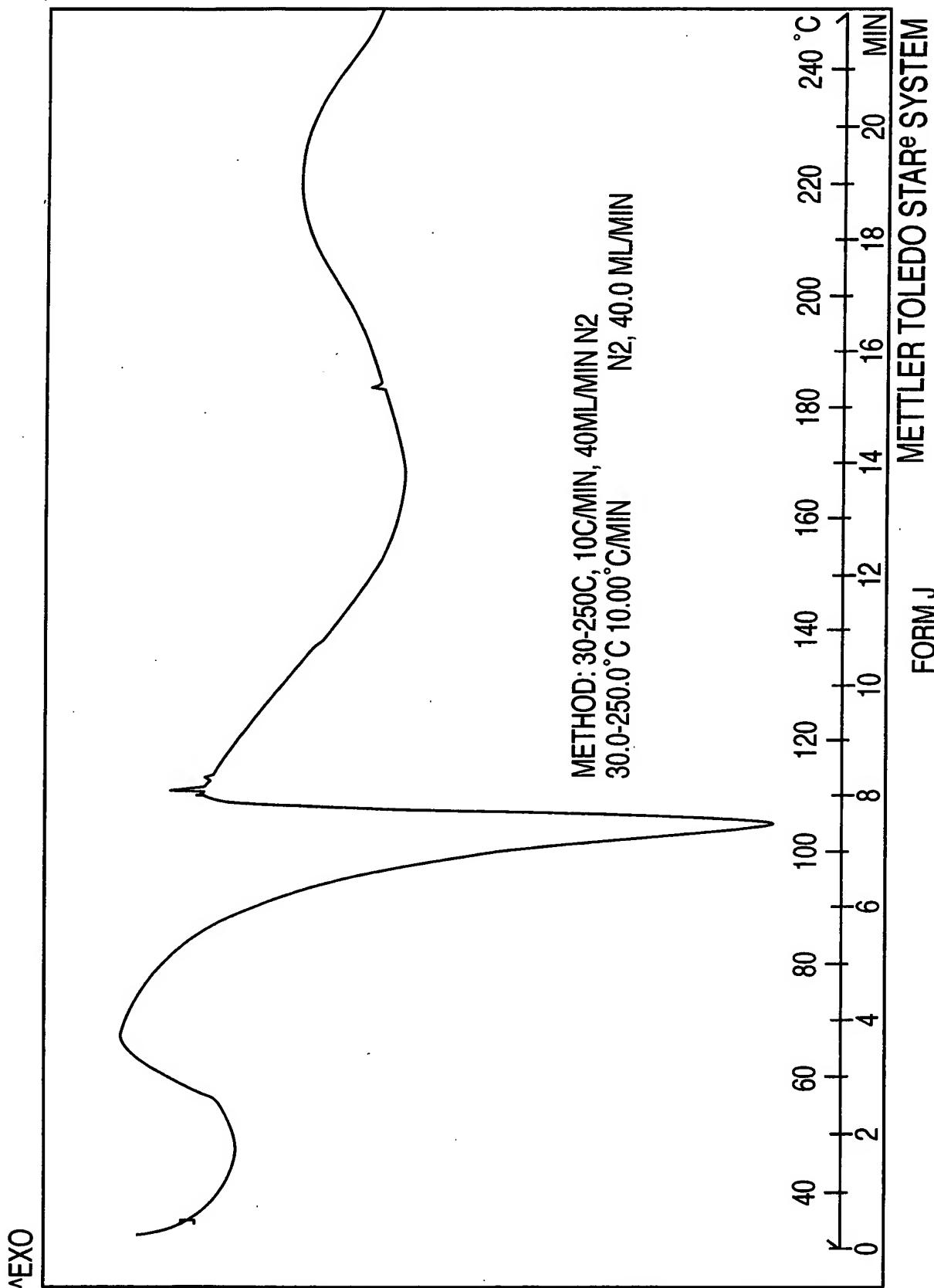
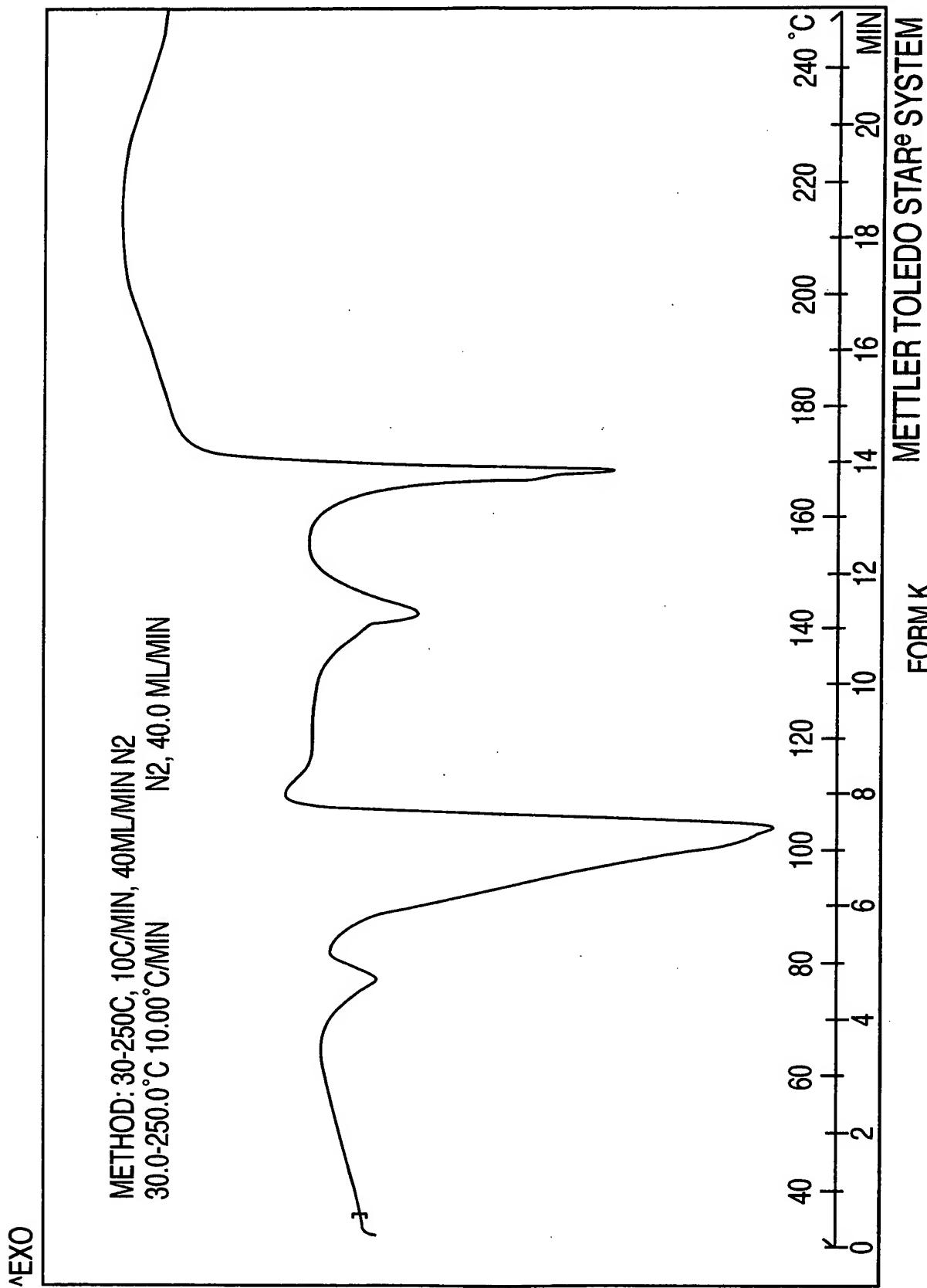
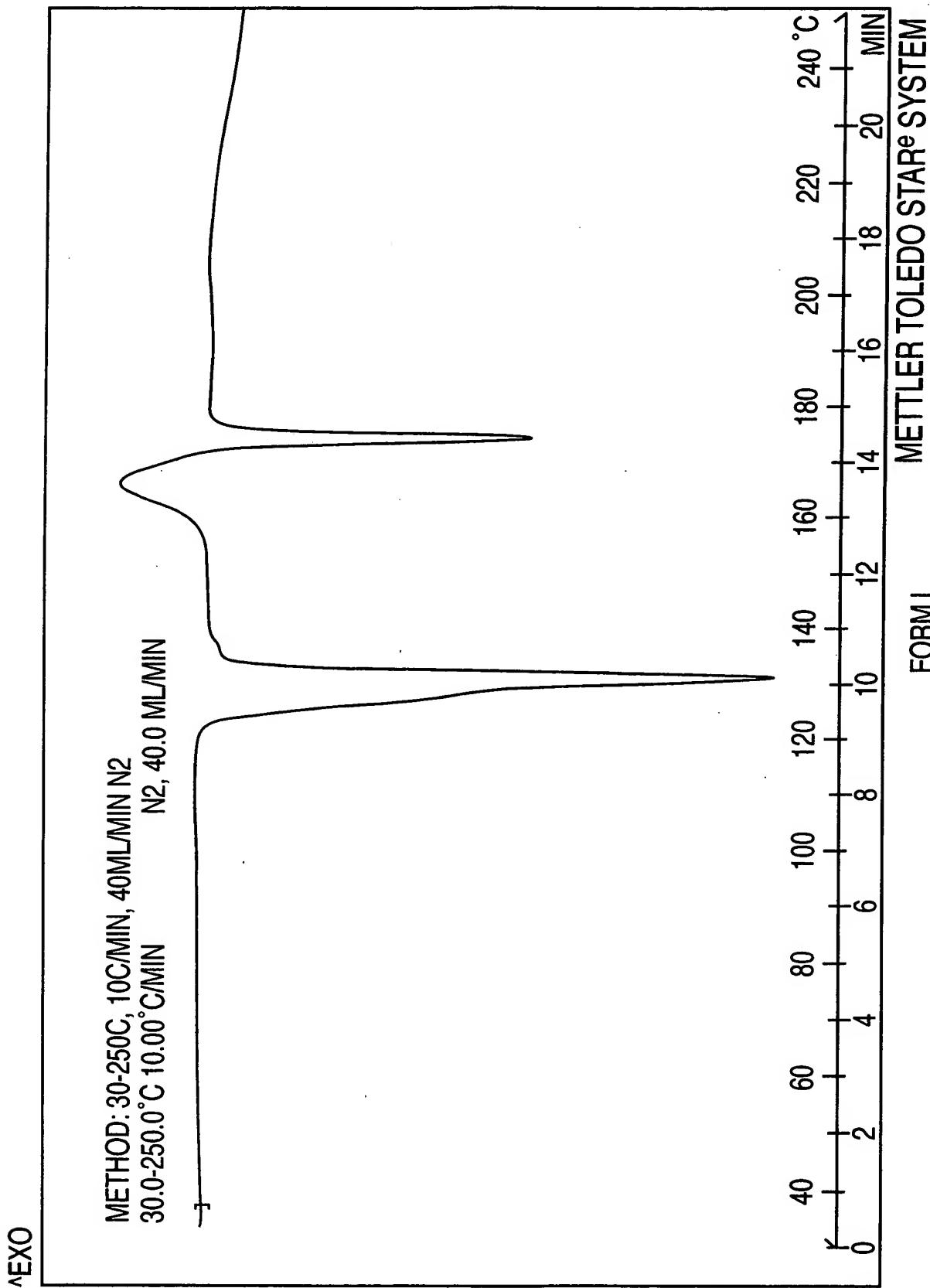


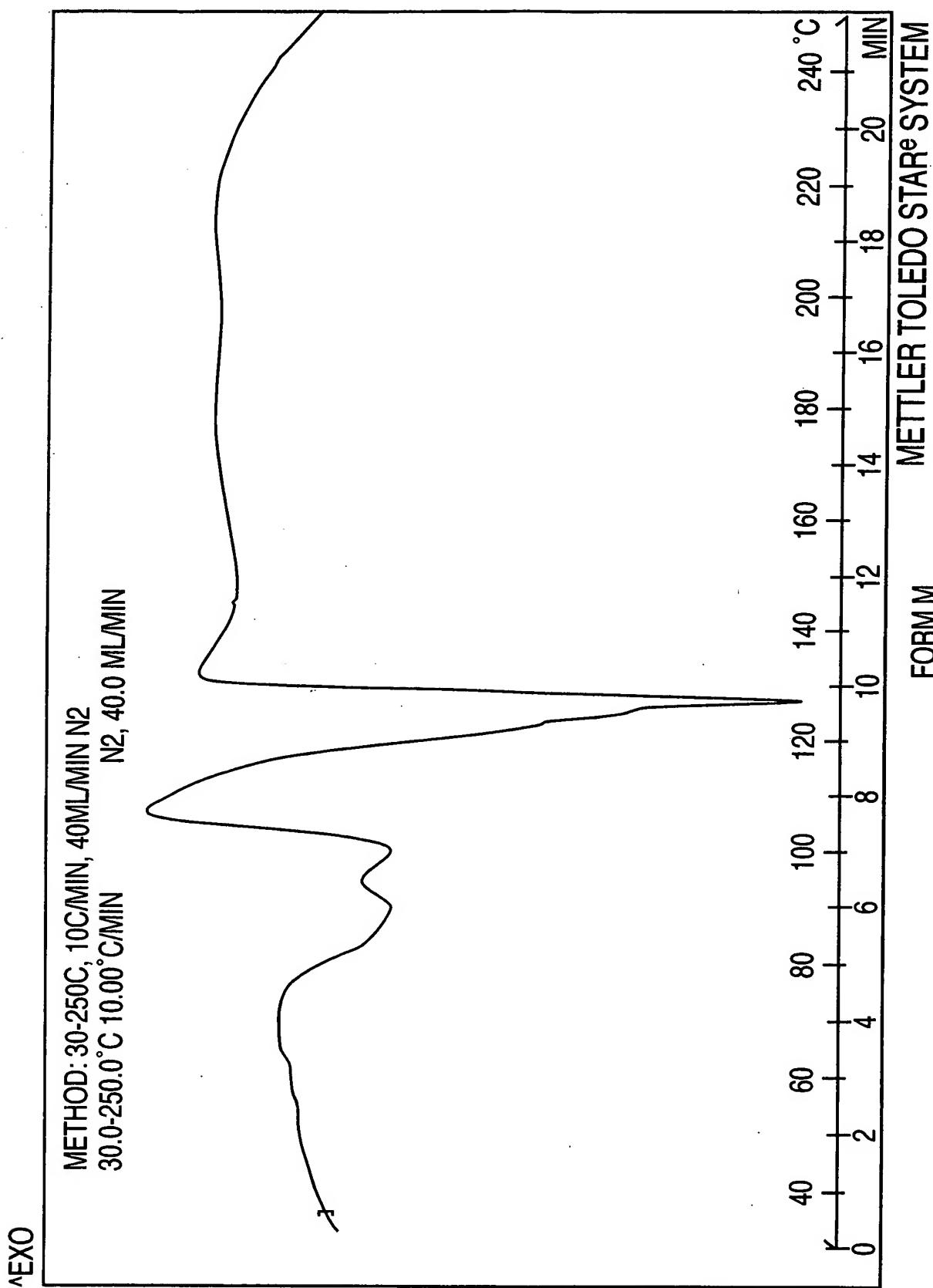
FIG. 40

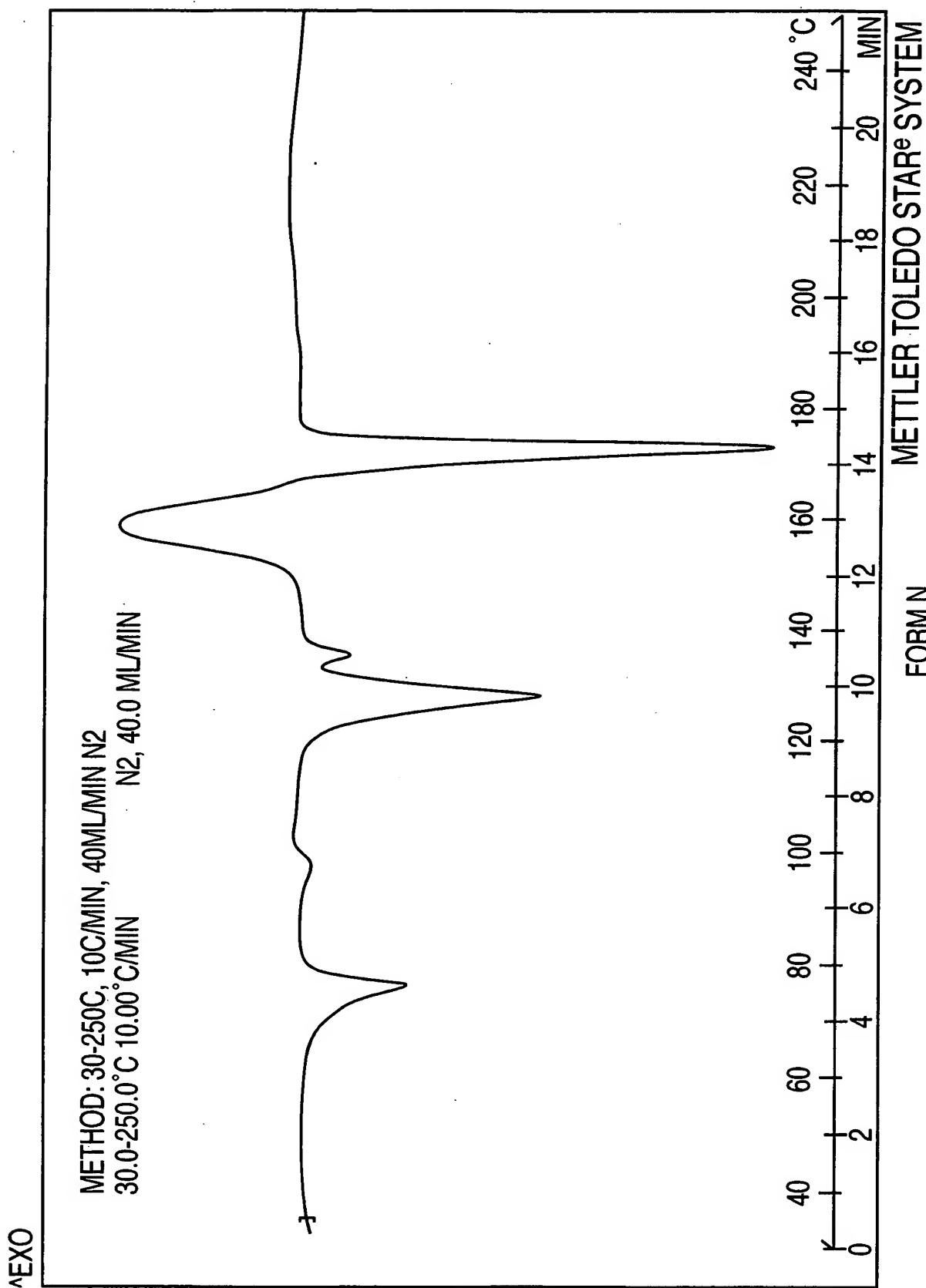


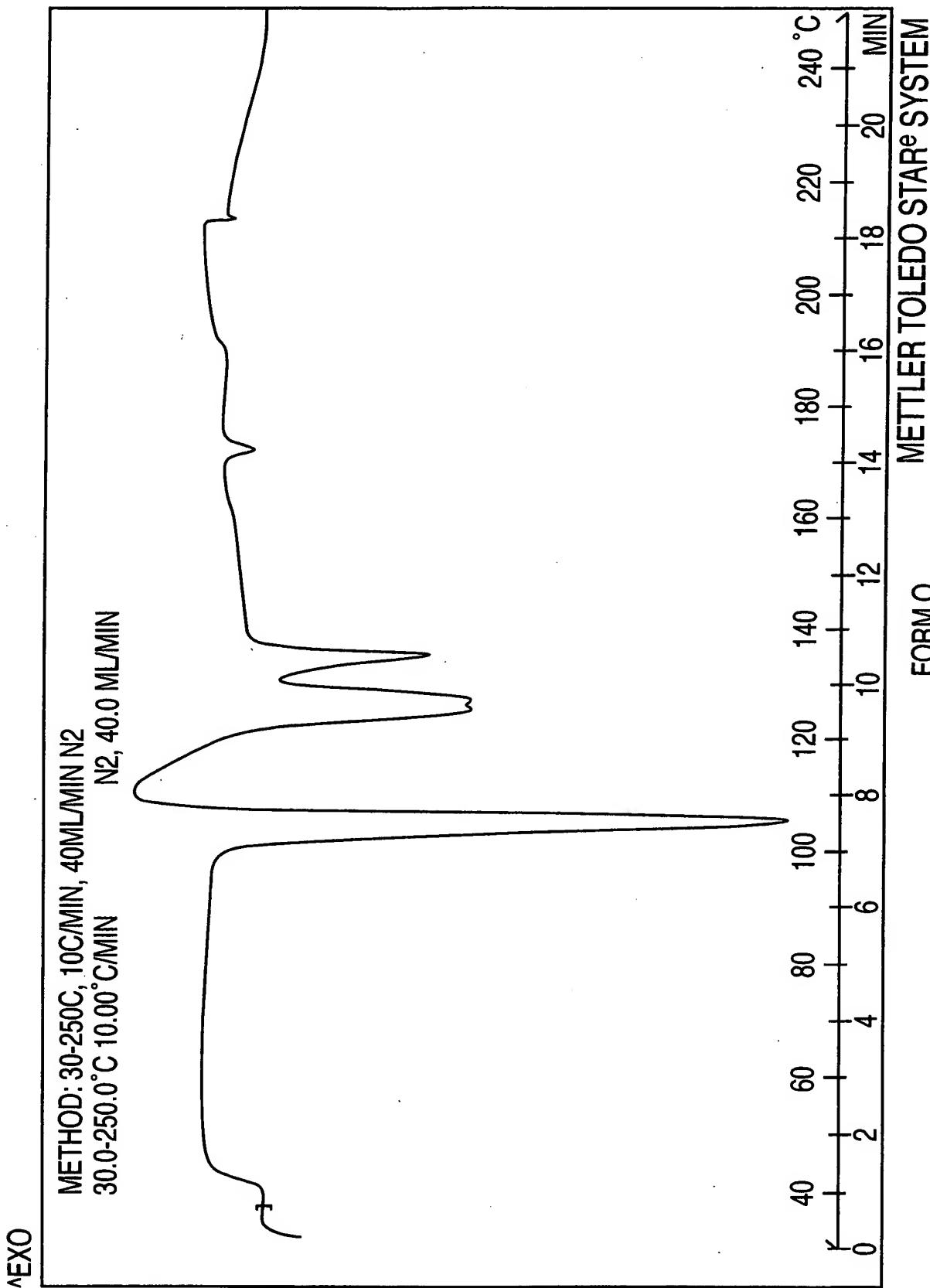












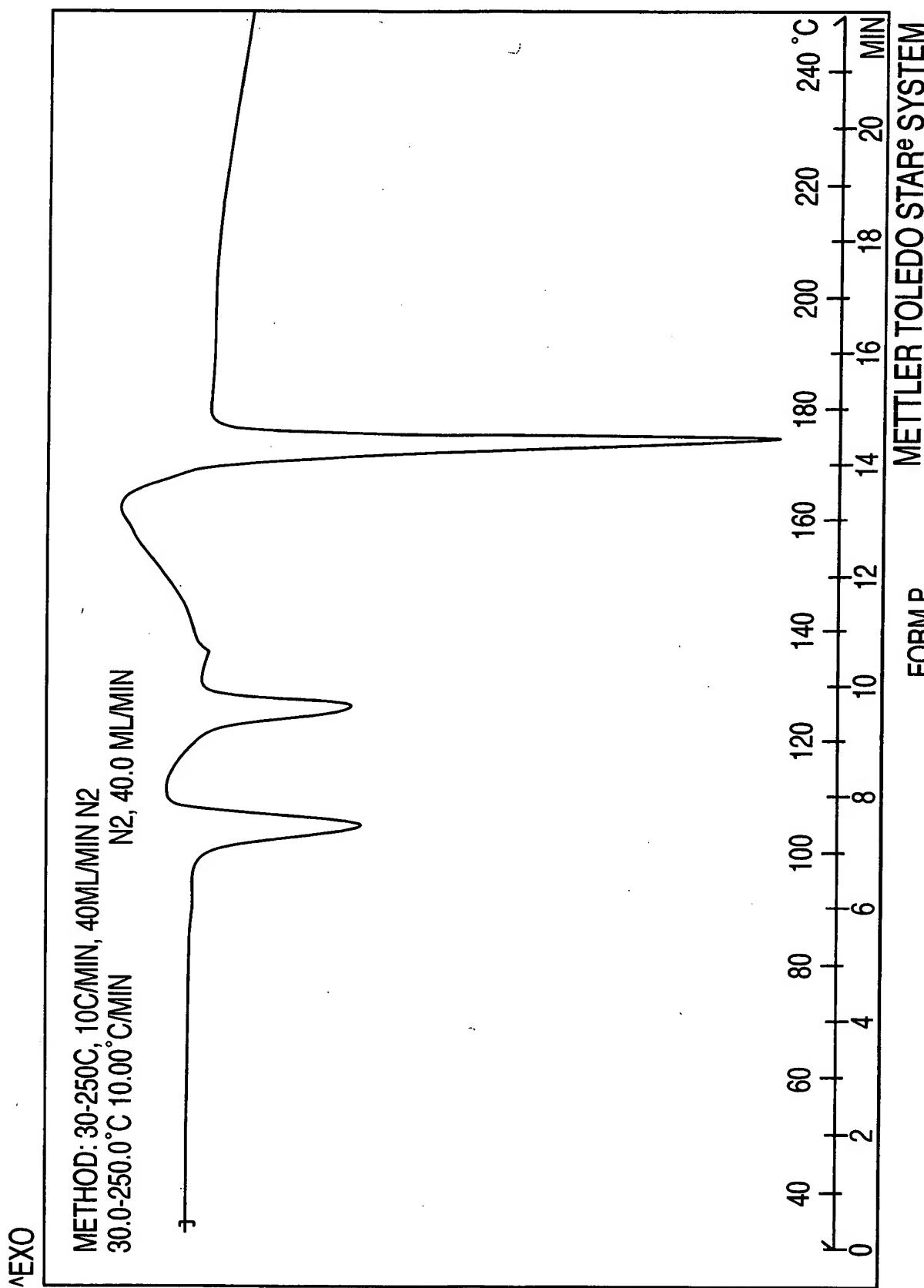
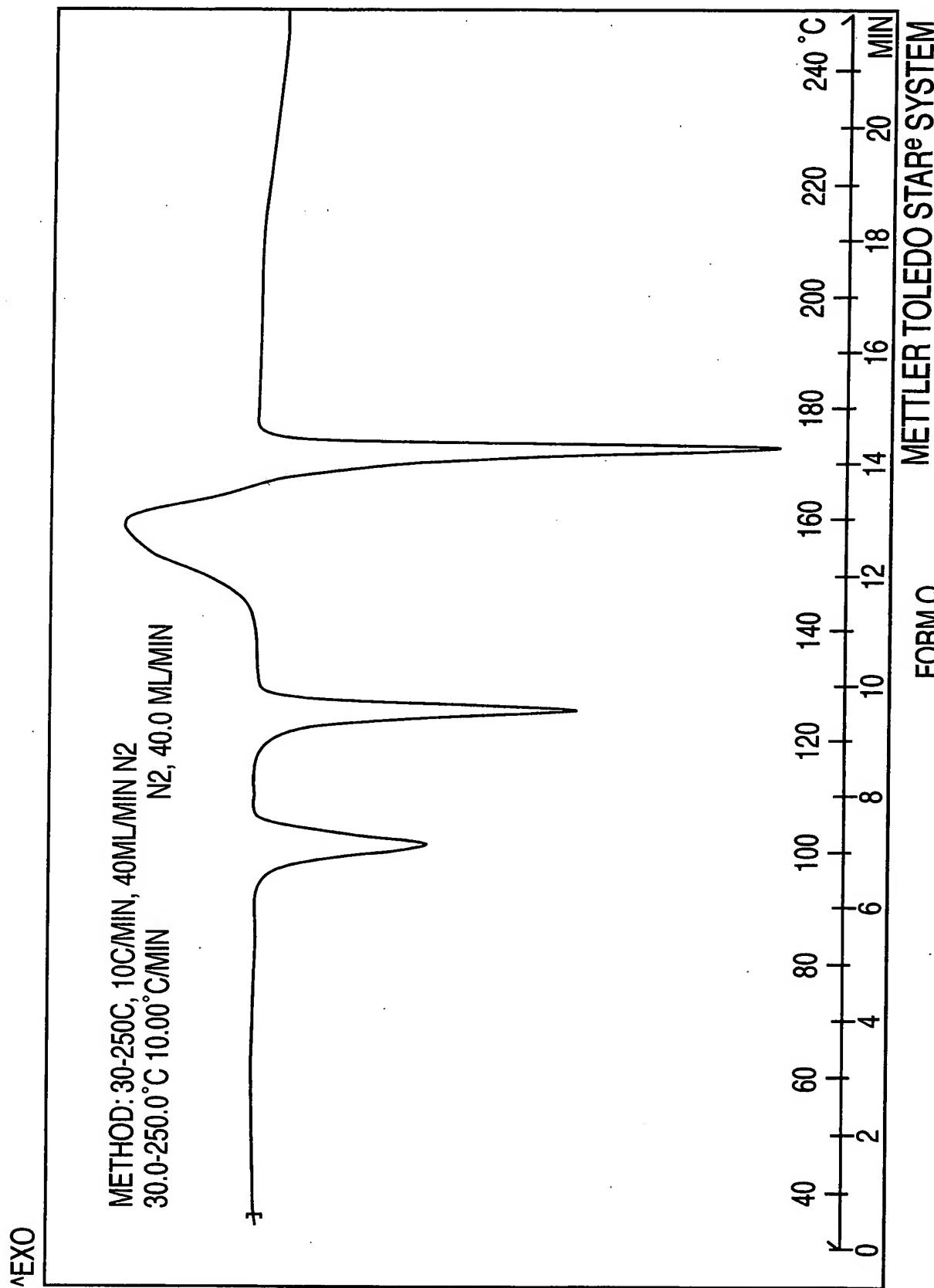


FIG. 48



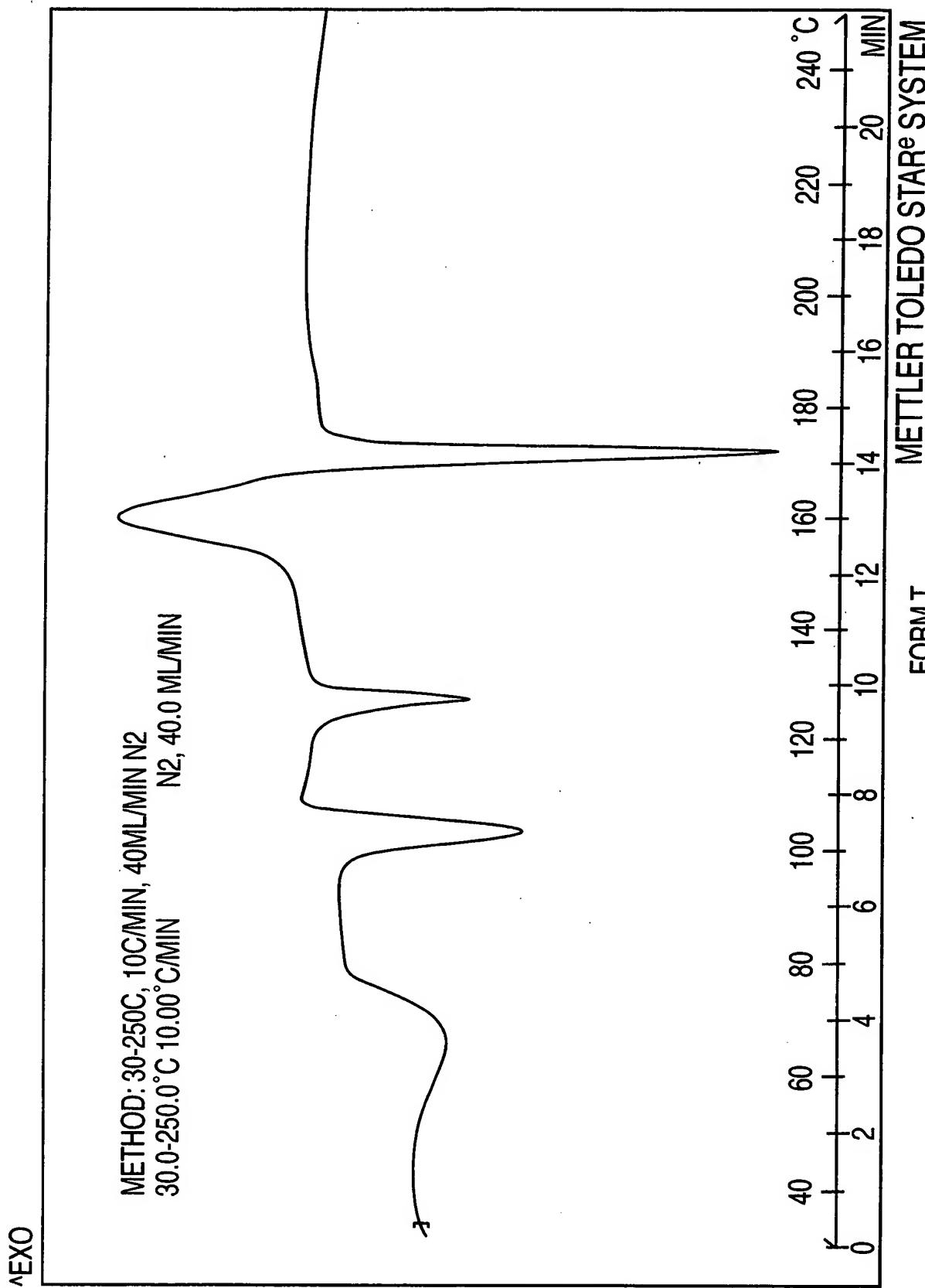


FIG. 50

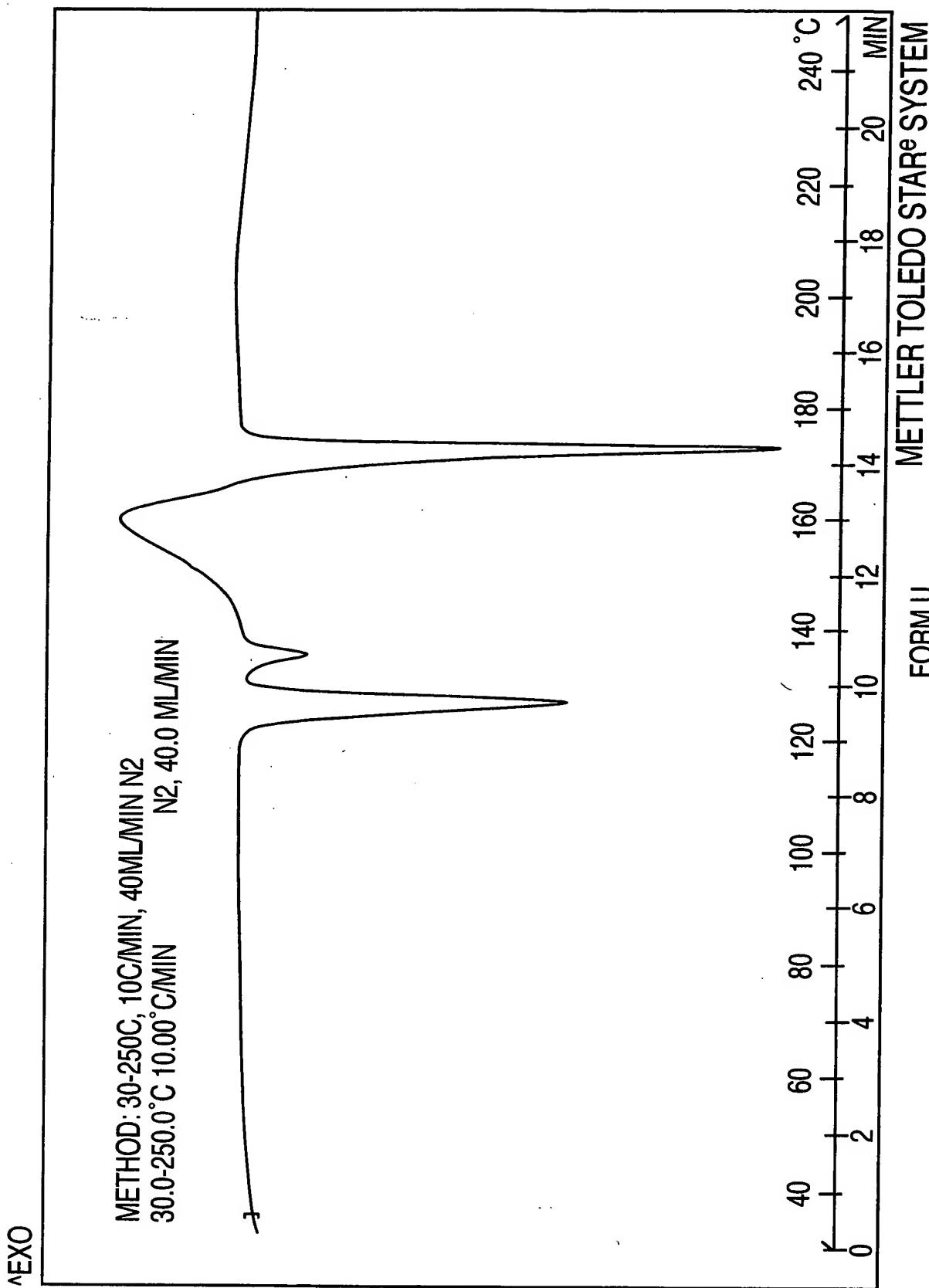
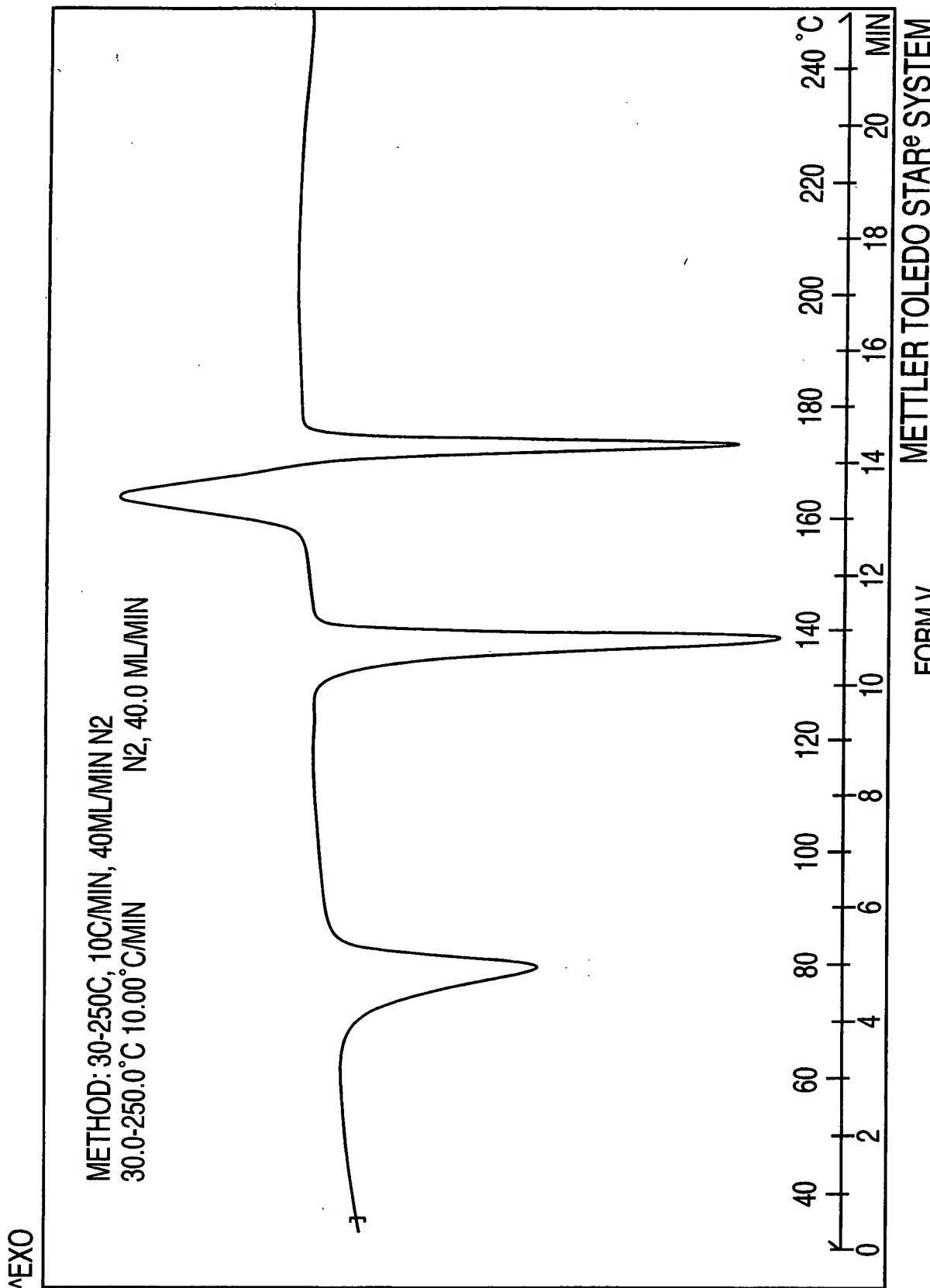


FIG. 51
FORM U



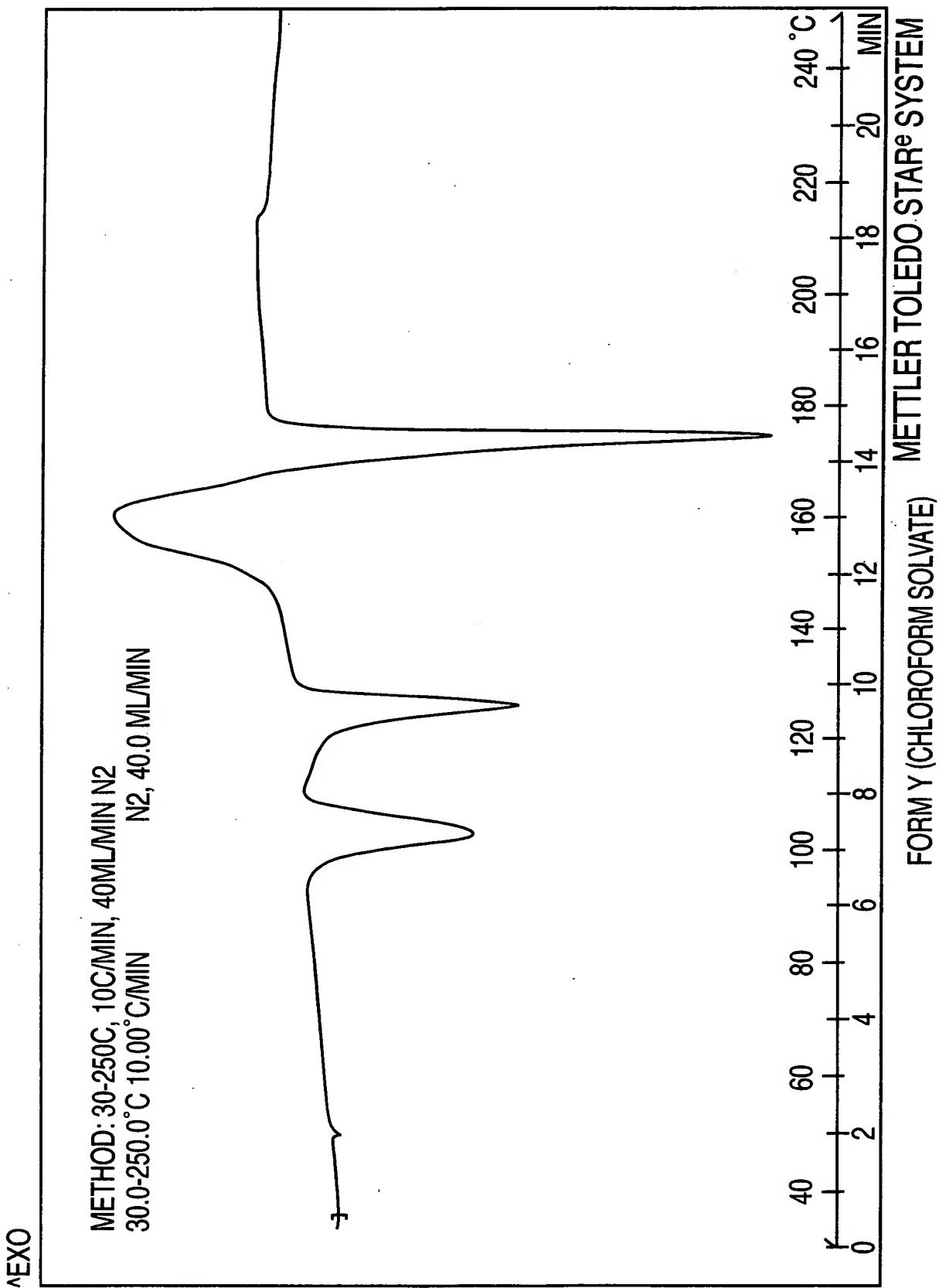
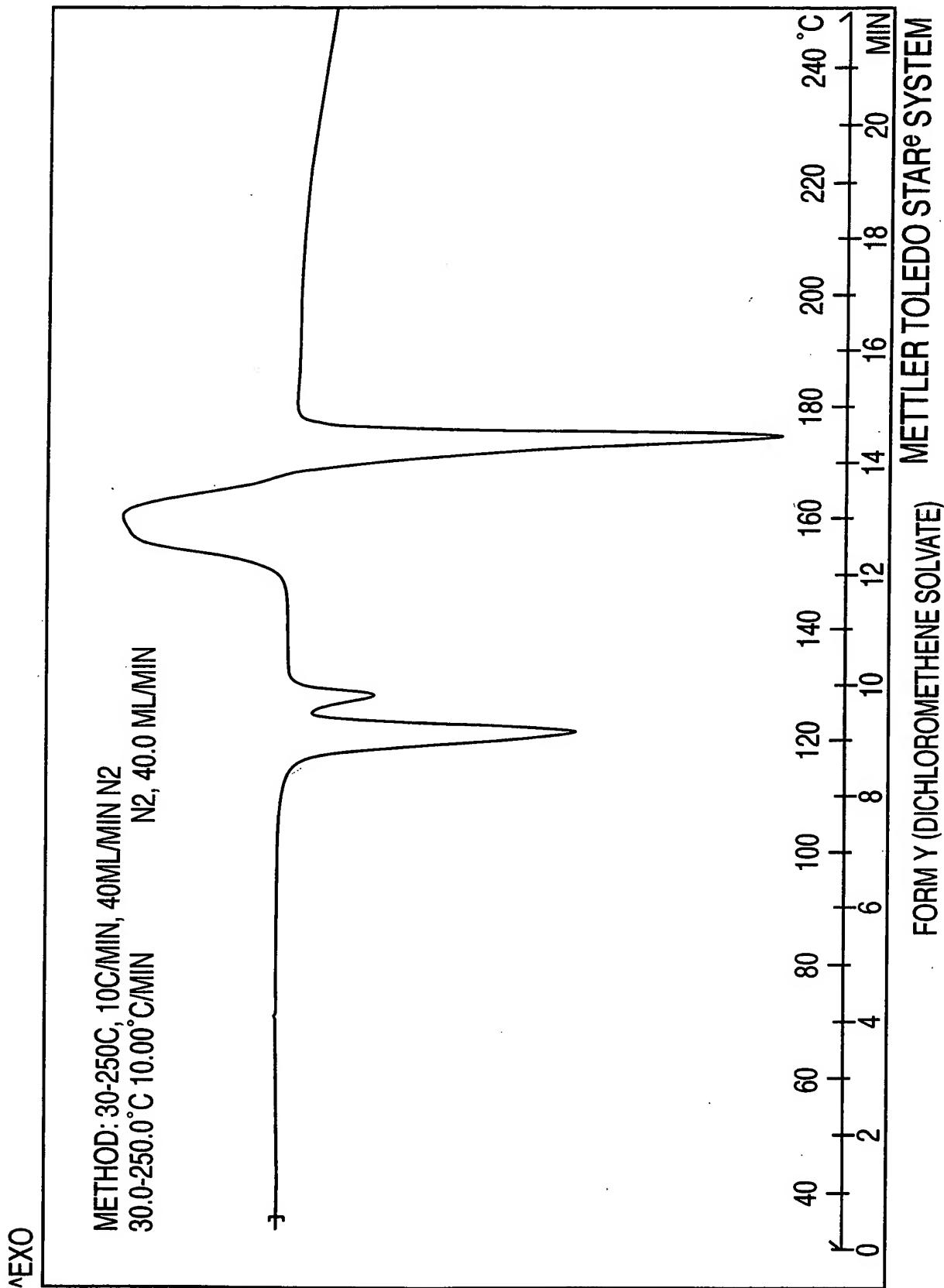
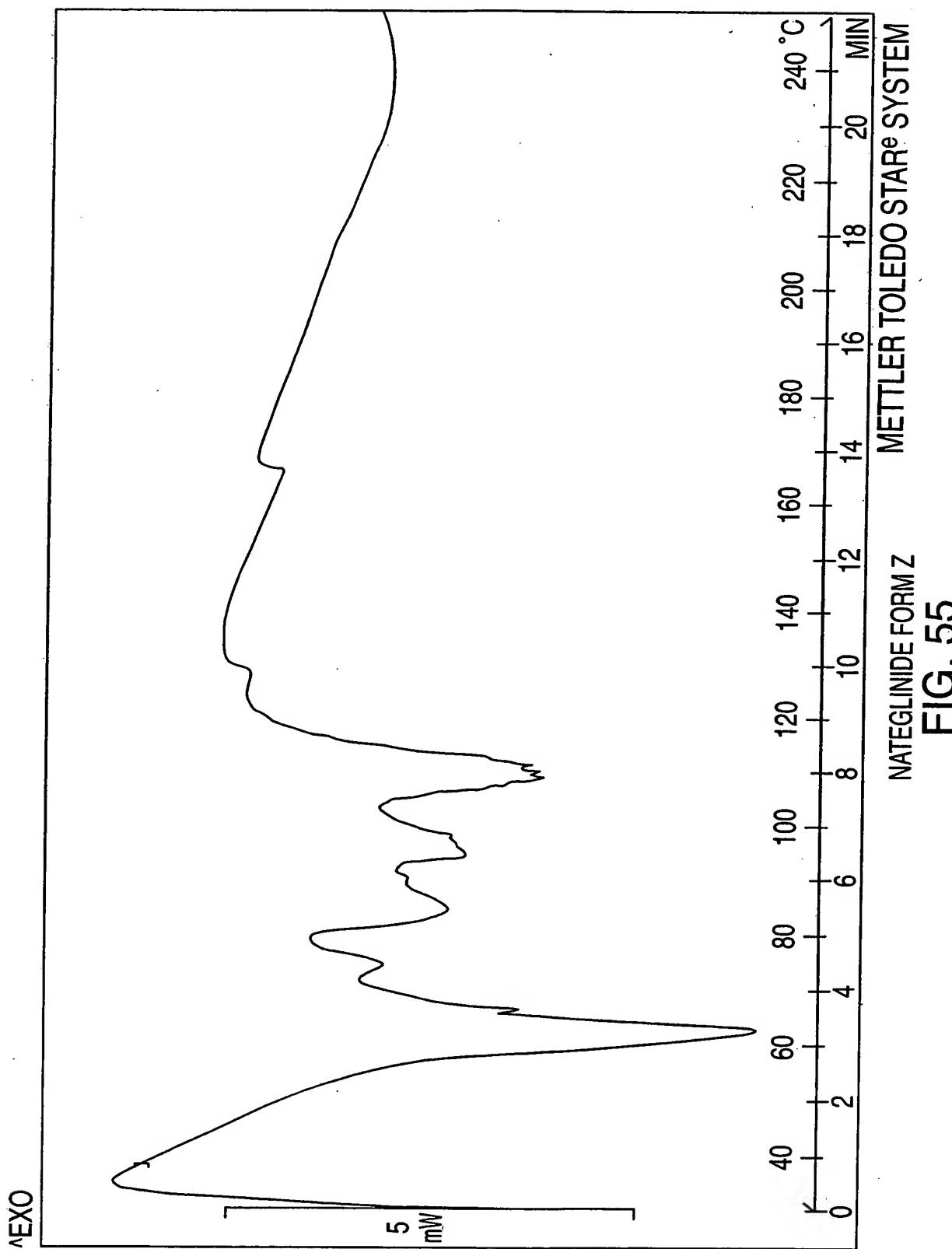
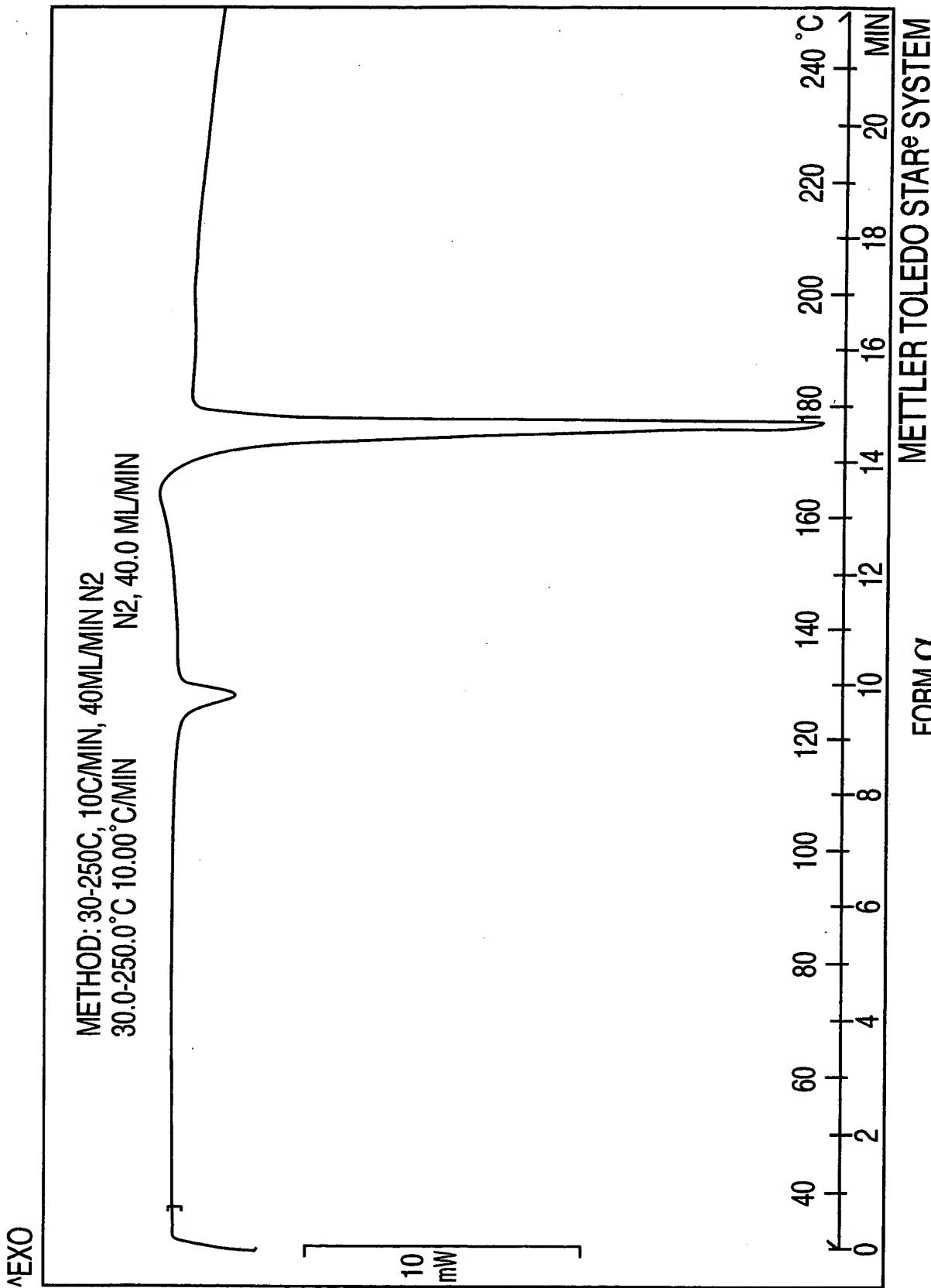


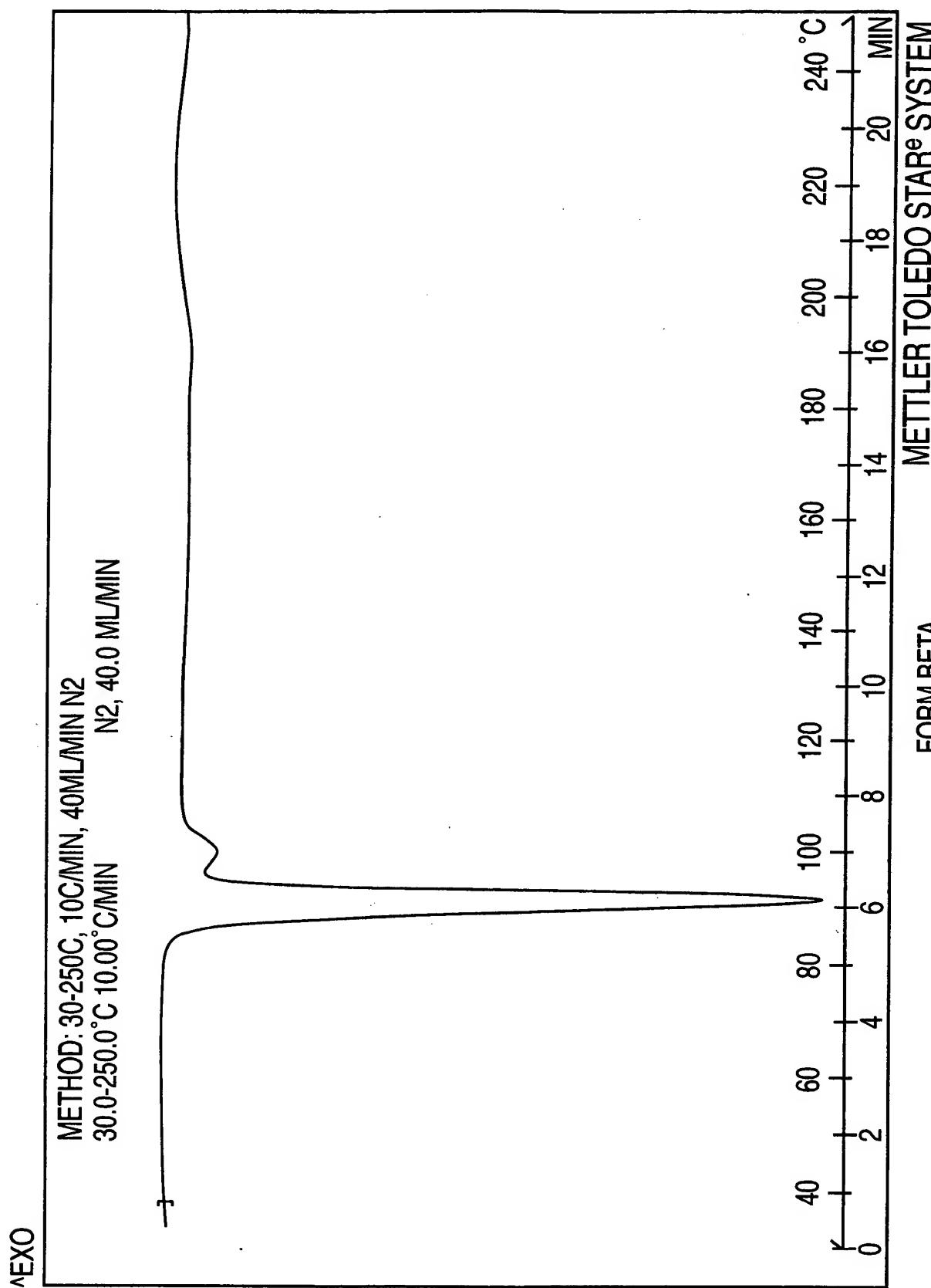
FIG. 53

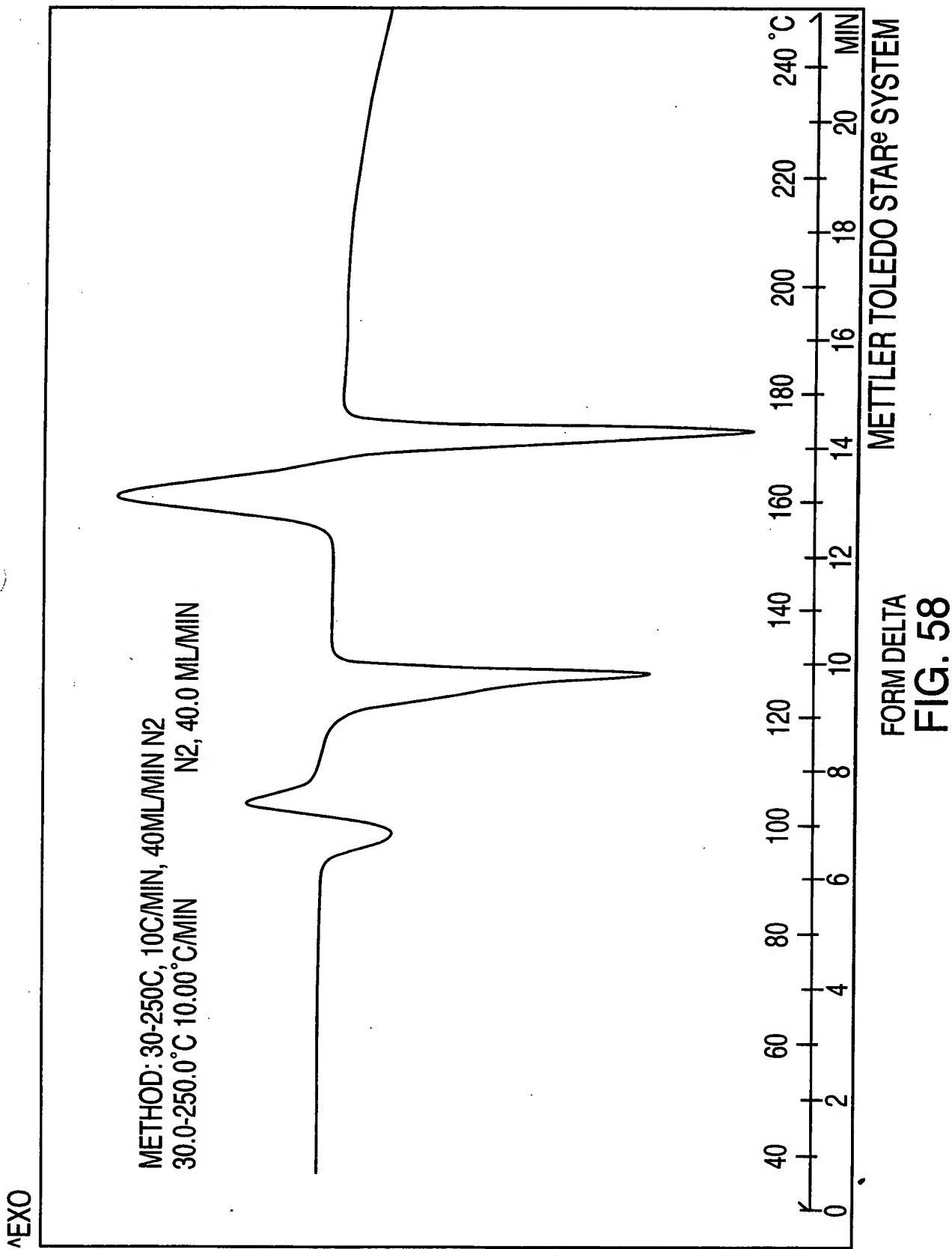






FORM α
FIG. 56





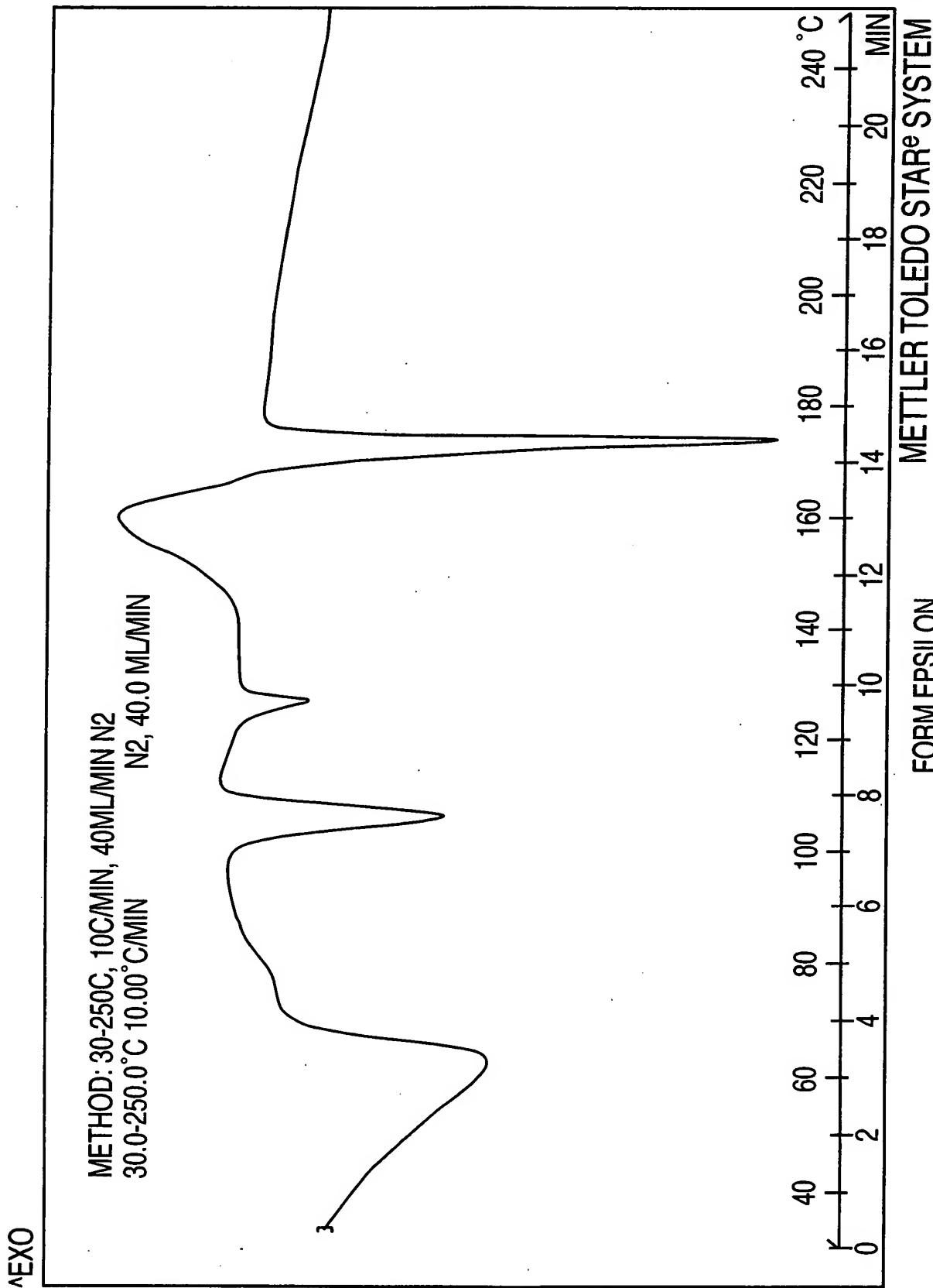
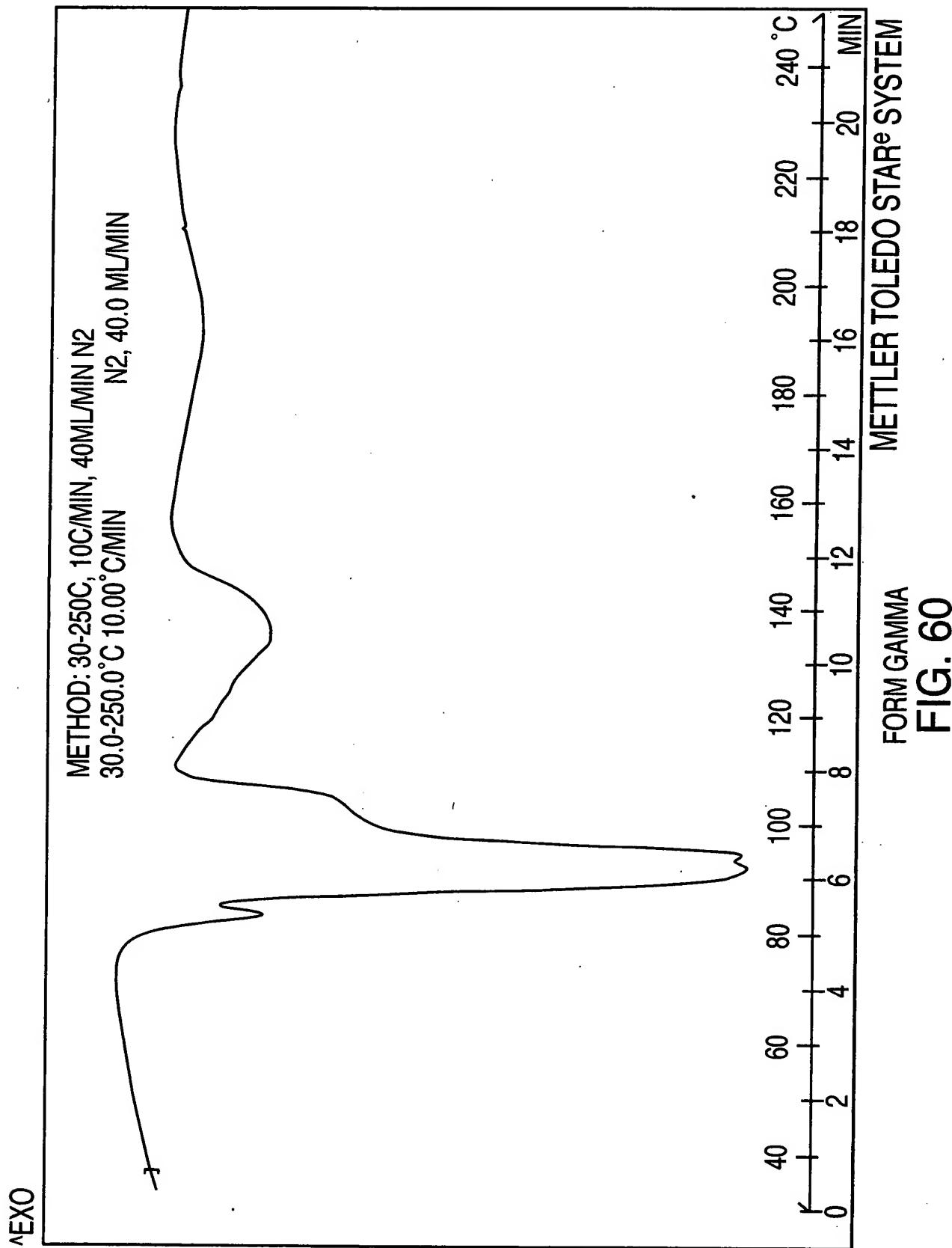
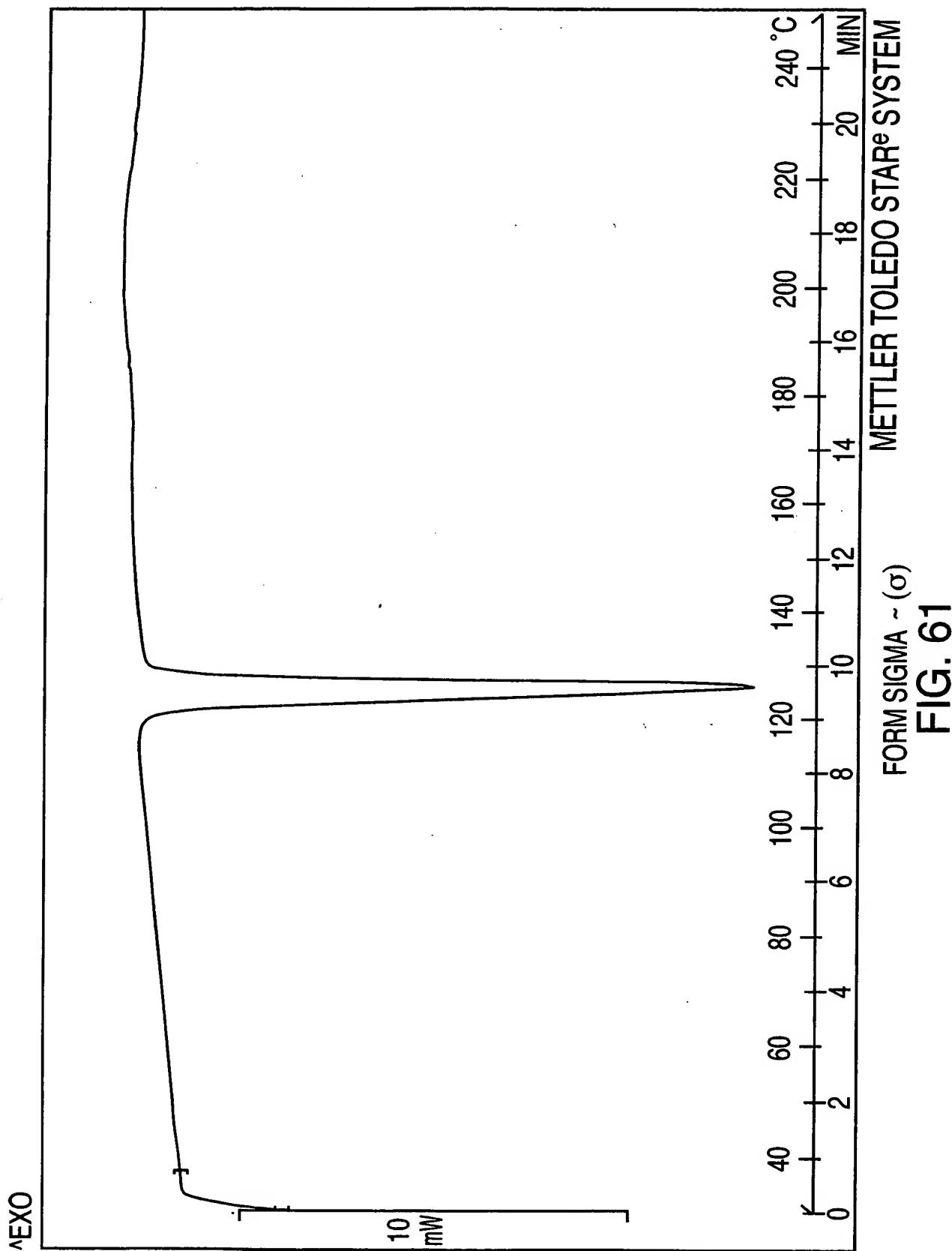
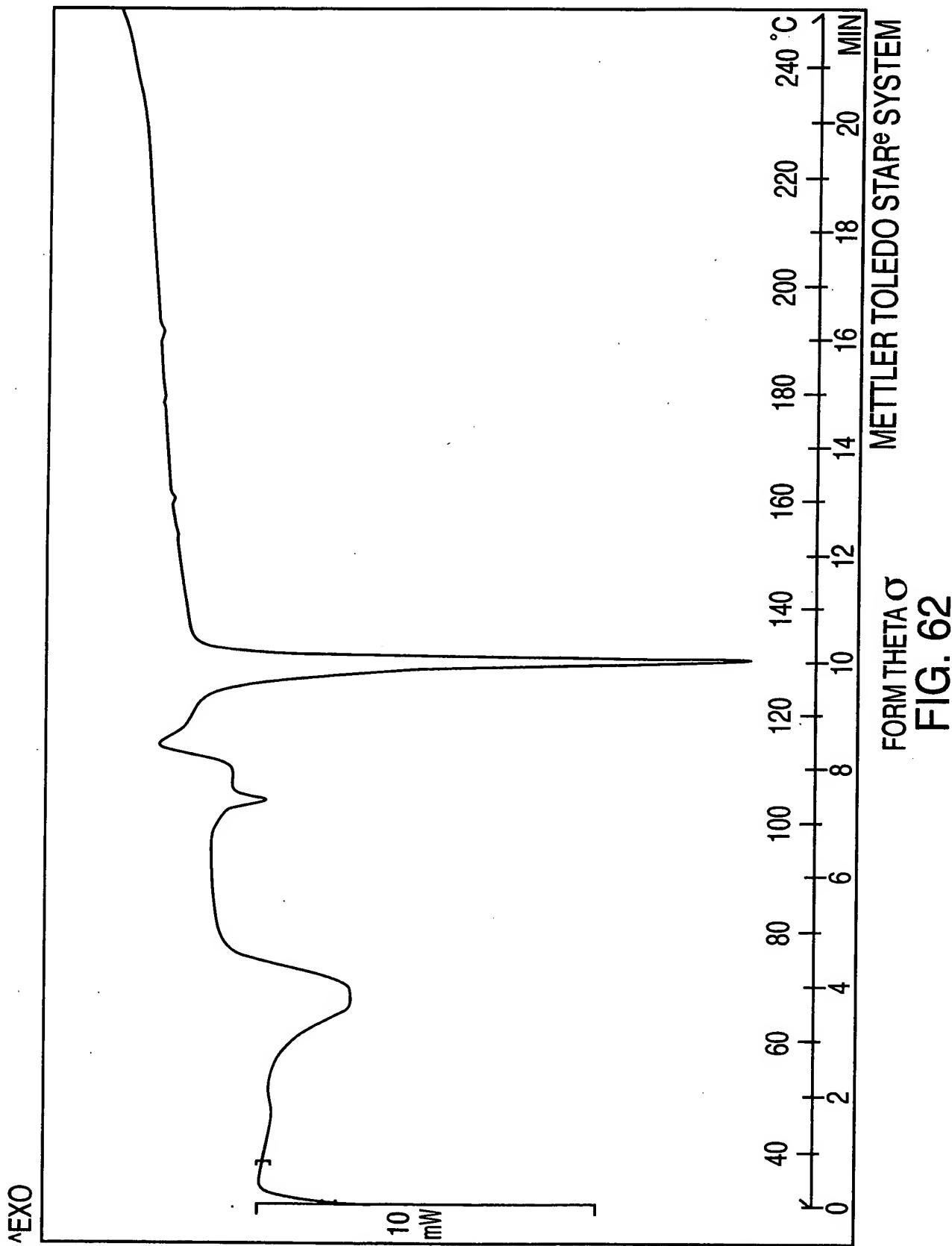
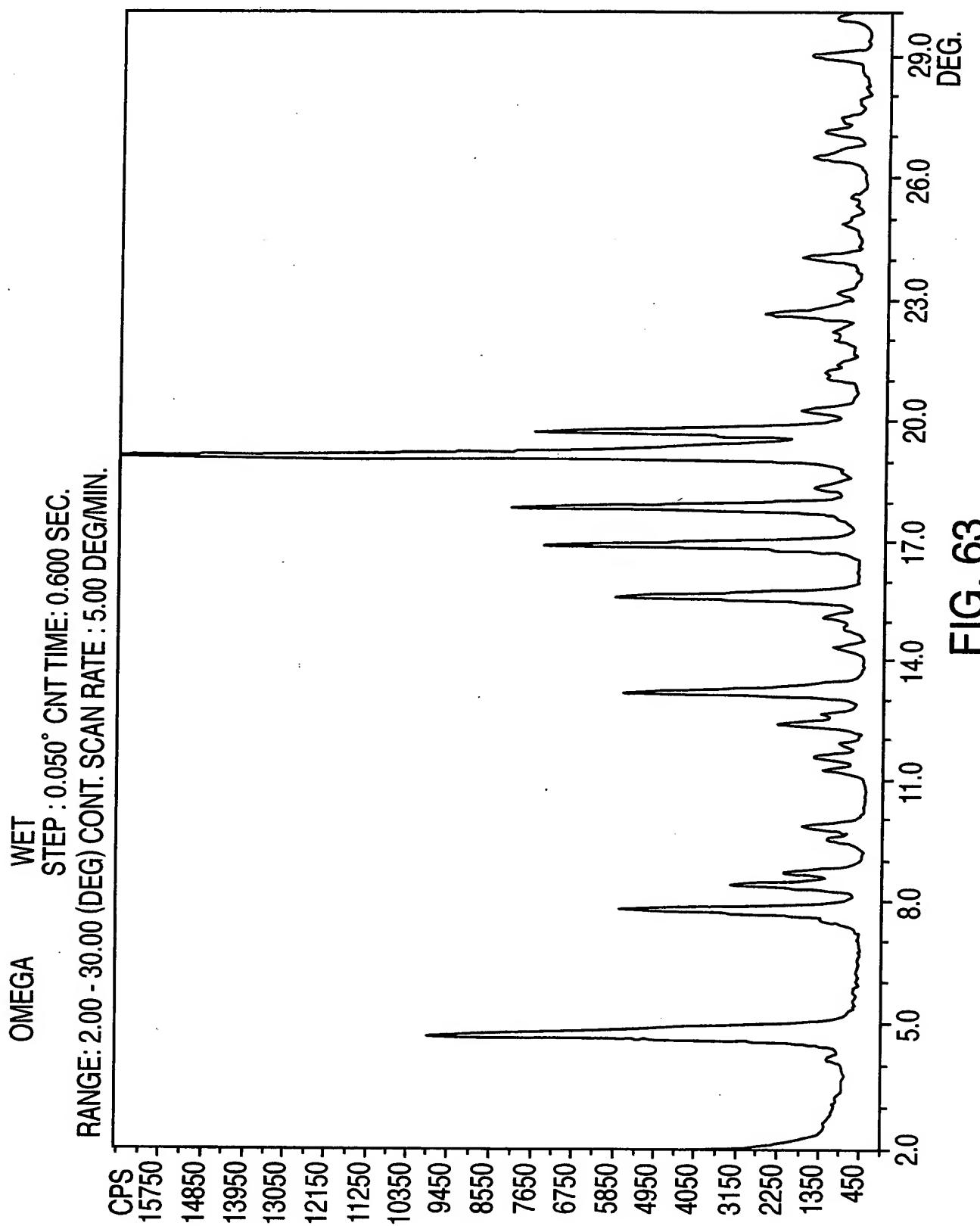


FIG. 59









Comparison between the impurity profile of Nateglinide crystallized in IPA-H₂O and Nateglinide in Methanol-H₂O

Sample No	Solvent	Impurity profile by RRT [% w/w]						
		D-PA (0.23)	(0.25) (0.46)	(0.80)	Ipcha (0.89)	Dimer (1.38)	Methyl Ester (1.51)	Isopropyl Ester (1.76)
RL-2155/1	Methanol-H ₂ O	<0.01	0.02	<0.01	0.03	0.02	2.91	0.04
RL-2163/4	IPA-H ₂ O	<0.01	0.04	0.02	0.02	0.01	0.03	0.02

Note: D-PA means D-Phenyl Alanine

Ipcha means Iso propyl cyclohexyl carboxylic acid

Both are the starting materials of the product

(-)-N-[(trans-4-isopropyl cyclohexane)carbonyl]-D-phenylalanine

FIG. 64